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announces

A Course In

Benign and Malignant Tumors

on

MONDAY, TUESDAY, and WEDNESDAY
APRIL 3, 4, and 5, 1939

A description of the course and an outline of the subjects to be covered will be found on pages 75-77.

GASTROSCOPY: ITS VALUE AND INDICATIONS

R. J. F. Renshaw, M. D.

Gastroscopy with the flexible gastroscope is a universally accepted diagnostic procedure and the indications for its use are well established. Opinions of leading gastro-enterologists throughout the world are in accord regarding the value of the procedure. Two well-known gastro-enterologists who have not been actively engaged in gastroscopy but who have watched its development are W. L. Palmer of the University of Chicago and Eusterman of the Mayo Clinic. Palmer[1] has said, "I am hopeful that the new method may be accorded the warm reception it so richly deserves by the conservative members of the profession and that it may be spared the fate of most new methods—overenthusiasm and exploitation by the more radical supporters. But this is too much to expect. I am confident, however, that gastroscopy will withstand the criticism of its adversaries, if there be any, and the exaggeration of its friends. It does not rival the x-ray examination; it is supplementary. The two methods have made the clinical study of gastric disease a definite objective science."

As Palmer correctly prophesized, there has been exploitation by radical supporters, criticism by adversaries, and exaggeration by friends, but gastroscopy has withstood all these, as is evidenced by Eusterman's statement in his introduction to the section of gastro-intestinal disease in the Yearbook of General Medicine for 1938. He states, "accumulating experience also attests the *indispensability* of competent gastroscopic examination in daily gastro-enterologic practice."

The criticisms which have been made of gastroscopy have been of two types. One has come from those who have not taken the trouble to learn about the procedure, or at least have become biased before they learned its indications and limitations. It is true that there have been five cases of perforation of the stomach but these all occurred when an experimental tip was used. The last case occurred in 1935 and this tip has now been discarded.[2] In not one case did complications develop and all the patients recovered uneventfully. No other perforations have been reported in this country or abroad and no deaths have been reported. Criticism of this type is made by those who contend that gastroscopy competes with roentgenology or that gastroscopy is useless because the roentgenologist can see shadows which mean more than the actual visualization of the gastric mucosa by the gastroscopist. Analysis of the facts, of course, disproves these contentions.

The second type of criticism has come from fair, open-minded adversaries and the conservative friends of gastroscopy who warn against overenthusiasm. They mention the difficulties and potential dangers

which may arise from gastroscopic examinations made by careless or poorly trained men. The technic is relatively easy to learn but the use of gentleness and skill are as important in carrying out this procedure as they are in any other diagnostic procedure, whether it be a digital rectal examination or "needling" of the eye. Schindler believes that the flexible gastroscope is safe "even in awkward hands" and so it would seem to be from the conspicuous lack of accidents. However, one need hardly mention the advantage of thorough training and adequate experience. To complement the examiner's skill, one needs an experienced assistant. This assistant must be one who can anticipate the examiner's movements and change the position of the patient's head in such a way that he experiences little or no discomfort. Some patients will complain of a pressure distress in the throat during the examination but only a few have a sore throat which persists for 12 to 24 hours. When carefully done most patients will willingly permit follow-up or recheck gastroscopic examinations. A good assistant will also prevent undue apprehension on the part of the patient. However, an assistant is not a necessity, because such expert gastroscopists as Benedict at the Massachusetts General Hospital and Taylor at St. Bartholomew's Hospital in London work successfully without an assistant. On one occasion it was necessary for me to examine without an assistant a very sick tuberculous patient on the kitchen table of his desert home in Arizona. Even under such conditions the patient experienced little discomfort and later requested a second examination.

Other criticism has dealt with orientation and interpretation of gastroscopic findings. There is no perfect diagnostic method and gastroscopists do not claim that gastroscopy is perfect. Certain areas of the stomach may not be seen by gastroscopy but these areas are not constantly invisible with two exceptions. A small portion of the juxtaesophageal area cannot be seen. The second blind spot is at the tip of the instrument but, by manipulation, this can be reduced to a small area. The other so-called blind spots may or may not be seen and with a varying degree of visibility. However, all blind areas together constitute only a small part of the total mucosal surface. The greater part of the stomach is usually well visualized. Interpretation of the gastroscopic findings involves a personal equation and requires much experience just as are required for cystoscopy, roentgenology, or any other observation.

A frequent point of discussion is how can the gastroscopist differentiate a benign from a malignant lesion or what is the evidence of gastritis. One should realize that the gastroscopist actually sees mucous membrane as other endoscopists visualize hollow organs and cavities. The stomach is distended, the blood and nerve supplies are intact, the

coloring is vivid, and the minute details stand out prominently. In any endoscopic method the examiner makes his diagnosis from what he *sees*. The microscopic examination, if biopsy can be obtained, only adds confirmatory evidence.

Indications for Gastroscopy

Negative Roentgen Findings

In anyone's practice there always is a certain number of patients who complain of chronic distress in the abdomen. In certain cases the roentgen examinations may have been reported as negative; yet, one still suspects some abnormality of the gastro-intestinal tract. Such patients have been estimated by various writers to constitute from 15 to 45 per cent of a practice. It is in this group that gastroscopy is of the greatest value and gastroscopists usually list this group of patients as the most important indications for gastroscopy.

Chronic gastritis is the most common organic cause of abdominal, or at least of upper abdominal, distress.[3] Fifty per cent of all patients examined by gastroscopy will have some form of gastritis according to the experience of both European and American authorities. Because the disease is so common and so distressing to the patient and because the practitioner wishes to make the correct diagnosis, chronic gastritis has been studied with the hope of finding some simple means of diagnosis. It is agreed that the symptoms are so varied and without a definite syndrome that while the presence of gastritis may be suspected, it cannot be made from the patient's history or without gastroscopic examination. Information from gastric analyses has been extensively studied in this group of cases.[4] It has been found that the acid secretion varied from achlorhydria with histamine through the normal range to "hyperacidity."

No type of secretory curve is characteristic of any type of gastritis or even of gastritis in general. In atrophic gastritis one may find normal or even high levels for the acid, while in superficial or hypertrophic gastritis one may find even an achlorhydria. The simplest accurate way to make a diagnosis of gastritis is to employ gastroscopy.

When the roentgen findings in gastritis have been compared to the gastroscopic findings, there has been no correlation between them. The roentgenologist seldom has been able to accurately make the diagnosis. In Schindler's experience, the roentgen diagnosis has been correct in but one case in 200. Others have had similar experiences. On the other hand, by direct inspection of the intact stomach—by gastroscopy —the diagnosis can be made accurately. Not only can one see the inflammatory reaction but it can be classified into chronic superficial, atrophic, or hypertrophic varieties, each of which bears a different prognosis and requires different management.

One may question the significance of mucosal changes which are said to be due to gastritis and certainly the lesser changes may well be doubted; but the marked inflammatory changes with redness, swelling, edema, erosions, ulcerations, or hemorrhages in a friable tissue can easily be seen. There is no doubt that such changes do cause symptoms and the symptoms are entirely relieved when the gastritis subsides.[5] The experienced gastroscopist will not emphasize the lesser changes but will make the diagnosis of gastritis only in the presence of obvious, well-marked changes.

Occult blood in the stools, melena or hematemesis may be due to a gastritis which has not been revealed by roentgen examination. When one sees how friable the inflamed mucosa may be and how easily it bleeds, one can well understand how a gastritis could be the source of occult blood or massive hemorrhage. The frequency of gastric erosions also demonstrates another possible source of bleeding. Some authorities, particularly in Germany, believe that 10 per cent of all cases of massive gastro-intestinal hemorrhage are caused by gastritis. The bleeding from a peptic ulcer or a gastric carcinoma is a well-known phenomenon. At times these lesions may not be revealed by roentgen examination; therefore, bleeding in the gastro-intestinal tract is an important indication for gastroscopy which should be done as soon as the evidence shows that profuse bleeding has stopped.

What has been said of bleeding is equally true of unexplained anorexia, low grade fever, nausea, vomiting, or weight loss. It has been my experience, as it has also been of others, that anorexia and loss in weight are fairly common complaints of patients with gastritis. One must also be on guard to recognize the possible presence of carcinoma in the presence of such complaints. Low grade fever to my knowledge is not a common finding in gastritis but it is in carcinoma. The cause of nausea or vomiting may be revealed by gastroscopy when other methods have failed.

It is obvious that when all the other established methods of examination reveal no abnormalities, many patients with vague or unexplainable symptoms have been considered to have gastric neurosis, psychoneurosis, nervous indigestion, functional dyspepsia, or some other equally incorrect diagnosis. We believe that true gastric neurosis is so uncommon that such a diagnosis is rarely, if ever, justified, and never justified without doing a gastroscopic examination.

Inconclusive Roentgen Findings

The second most important indication for a gastroscopic examination is incomplete, inconclusive, or inconsistent roentgen findings. In this

group the examination is probably most important and is used most commonly following operations on the stomach. In such cases the roentgen findings very frequently leave some doubt concerning the true condition. Marginal or jejunal ulcers are not as well demonstrated as gastric or duodenal ulcer and the roentgen examination may give essentially negative findings but many patients will still have symptoms of ulcer. Because one can usually see almost the entire stomach by gastroscopy, direct visualization by this means becomes a valuable adjunct to the examination. The stoma is usually well seen and any ulceration in or near the opening stands out clearly. A very large number of patients will have a severe mixed type of gastritis following gastric operations. This is rarely detected without a gastroscopic examination.

Deformity of the duodenal bulb without a demonstrable crater or niche may be considered an insufficient or inconclusive finding. The deformity alone, even with symptoms simulating ulcer, constitutes an indication for gastroscopy because ulcerative gastritis may be the cause of symptoms and the duodenal deformity be but an inactive remnant of a previous ulcer. In fact, duodenal ulcer itself is an indication for gastroscopy to confirm or exclude the presence of concomitant gastric disease. Certainly, in any duodenal ulcer for which one contemplates gastric surgery, a gastroscopic examination is warranted first. The presence of gastritis may interfere with the proper function of a new gastric outlet or otherwise impair the physiology of the stomach.

Under the heading of inconclusive findings, one would consider bizarre filling defects, benign tumors, defects suspected of being extragastric, suspected gastric syphilis, suspected lymphogranulomatous disease of the stomach, and other uncommon conditions.

Gastric Ulcer

Every gastric ulcer should be examined by gastroscopy and not once but two or more times. The reason for this is obvious. By direct visualization of the ulcer, the gastroscopist is able to confirm the roentgen diagnosis, but more important, he can accurately observe the healing of the ulcer. It is a well-known phenomenon that the niche seen by roentgen examination may disappear very rapidly after treatment has been instituted. The disappearance of edema about the ulcer has been offered as an explanation for such rapid reduction of the size of the niche. To my knowledge the most rapid time for complete epithelialization, as observed by gastroscopy, of a gastric ulcer has been five weeks, and seven or eight weeks is the usual period. However, some cases will require a longer time. Palmer, Schindler and Templeton[6]

observed some cases with delayed healing, in one of which an ulcer persisted for a year and another patient had a persistent or a recurrent ulcer over a two year period. Their study emphasizes the need for doing both roentgen and gastroscopic examinations when following the course of an ulcer. The ulcer is not always visible at the same time by both methods. The lesion may be visualized by gastroscopy and not by the roentgen ray at one time and vice versa at another time. When doing both gastroscopic and roentgen examinations, there may be a question of which procedure should be done first. Since the real contraindications for gastroscopy may be suspected from the history and physical examination or detected by fluoroscopy of the chest which is always done before making a gastroscopic examination, the latter may precede or follow the roentgen examination. We prefer to have the roentgen study done first, but this is not always feasible. Small flecks of barium may adhere to the mucosa for a day or two after the ingestion of the barium meal and it is possible for barium to remain in an ulcer crater for several days. Because of this fact, gastroscopic examination is rarely carried out in less than two days following roentgen examination and then if there is any question of malignancy of the ulcer, we have the patient's stomach thoroughly lavaged and repeat the gastroscopy the next day.

If the patient lives a long distance from the doctor's office or if time is a vital factor to the patient, gastroscopy should be done before the roentgen examination providing, of course, there are no obvious or questionable contraindications. It should be emphasized that an Ewald tube is always passed before the gastroscopic examination. If any obstructive lesion of the esophagus is present, it will be detected with the Ewald tube and the gastroscopic examination would not be done. Even if the Ewald tube passes successfully, but one encounters resistance with the gastroscope, the examination is discontinued immediately. Certainly, all follow-up gastroscopic examinations should be done before the roentgen study. On the other hand, if a patient comes to us solely for a gastroscopic examination, we insist that the patient bring with him recent roentgen films as well as all other data pertinent to the problem.

Gastric Carcinoma

A gastroscopic examination should be made in all cases where carcinoma is suspected but has not been demonstrated by the roentgen ray. In known cases it should be performed before operation for two reasons: to confirm the diagnosis and to help determine the mucosal extent of the pathological changes. It has been shown that involvement of the mucosa alone is rarely, if ever, detected by the roentgen ray. In a similar

manner it has been shown that inspection and palpation of the tissue at the surgical table does not correspond to what the gastroscopist sees. A point overlooked by most critics and not appreciated by those who have never observed the stomach through the gastroscope is that the gastroscopist sees an *intact, living* stomach as no one else has the opportunity to see it.

The endoscopic diagnosis of malignancy or benignity is the same in any method—it is based on what the endoscopist sees and biopsy adds but confirmatory evidence. Without biopsy, the endoscopic diagnosis is quite accurate and the inability to obtain biopsy is not a drawback. The gastroscopist, then, can in a very high percentage of cases, make an accurate diagnosis. This is particularly true of ulcerating lesions. On the other hand, a small, localized, nonulcerative infiltration may be hard to detect. However, by using both the roentgen and gastroscopic examinations, the diagnosis should be accurately made in nearly every case. Having made the diagnosis, the gastroscopist is of value to the surgeon by determining the mucosal extent of the process. Lesions which have been regarded as inoperable because the infiltration seemed to extend too high for successful surgery have been proved by gastroscopy to be operable. The reverse situation has also been observed; gastroscopy has revealed that the pathological process was too extensive and the patient has been spared an unnecessary laparotomy. Just as important as a preoperative examination is a postoperative examination. Just as the cystoscopist does repeated cystoscopies to watch for recurrences, so does the gastroscopist advise frequent gastroscopies to discover early recurrences of the disease. The same logic applies to roentgen therapy follow-up examinations.

Miscellaneous Conditions

Included in this group are the deficiency diseases, pernicious anemia, blood dyscrasias, allergic states, skin diseases, and the lymphogranulomatous diseases. Already, interesting information is being accumulated on the presence of and the relation of mucosal changes to deficiency diseases. For instance, I have seen a case of early carcinoma which was found by the gastroscopist during his routine examination of a patient with pernicious anemia. The French workers have reported finding gastric changes in lichen planus, chronic urticaria, and certain other skin conditions. They also report gastric changes in allergic conditions. Lymphosarcoma of the stomach has been observed by gastroscopic examination, and gastroscopy may be an aid in differential diagnosis.[7]

GASTROSCOPY: ITS VALUE AND INDICATIONS

Summary

1. Gastroscopy with the flexible Wolf-Schindler gastroscope in skilled hands is a safe, simple, practical office procedure which yields valuable information about the human living stomach and this information is obtainable in no other way.

The following are the established indications for gastroscopy at the present time:

I. Patients with negative gastro-intestinal roentgen findings but in whom one still suspects gastro-intestinal disease as:

(1) Chronic abdominal distress or pain
(2) Hematemesis
(3) Occult blood in the stools
(4) Loss in weight
(5) Nausea and/or vomiting
(6) Diarrhea
(7) Unexplained low grade fever
(8) Anorexia
(9) Anemia

II. Patients with inconclusive or inconsistent roentgen findings as:

(1) Postoperative stomach (resection and gastro-enterostomy)
(2) Bizarre or questionable filling defects
(3) Questionable benign tumors
(4) Questionable syphilis of the stomach
(5) Question of extra- or intragastric lesions
(6) Deformed duodenal bulb without niche or crater.

III. Gastric ulcers

IV. Gastric carcinoma

Miscellaneous conditions as deficiency diseases, anemias, lympho-granulomatous diseases, allergic states, certain skin conditions, and blood dyscrasias are not established indications but gastroscopy has proved helpful in their diagnosis.

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BEDSIDE RECOGNITION OF THE DISTURBANCES OF CARDIAC RHYTHM

A. Carlton Ernstene, M. D.

Present day knowledge of the disturbances of heart rhythm is based primarily upon earlier studies of the arrhythmias by means of the polygraph and the electrocardiograph. Correlation of the results of these studies with careful clinical observations has now made it possible to differentiate most of the arrhythmias at the bedside without instrumental aid. The electrocardiograph is, of course, an instrument of great value but its field of greatest usefulness no longer has to do with the disturbances of cardiac rhythm. Electrocardiograms should be made in every case of actual or suspected organic heart disease but, for the experienced observer, the recording of abnormal heart rhythms in this manner usually will serve only to corroborate an earlier clinical diagnosis. Even in these cases, however, the tracings may give additional information of importance, and for the detection of certain disturbances of rhythm, graphic registration remains indispensable.

Sinus Arrhythmia

In any discussion of the irregularities of heart rhythm, mention should be made of sinus arrhythmia. In this condition there is a gradual increase in the heart rate during inspiration and a corresponding decrease during expiration. The disturbance is encountered commonly in children and is a usual finding in individuals who have neurocirculatory asthenia. It may also develop as a manifestation of digitalis overdosage, and this is the only situation in which it becomes of clinical importance. Sinus arrhythmia often can be accentuated by slow, deep breathing and abolished by exercise.

Premature Beats

Except for sinus arrhythmia, the most common disturbance of cardiac rhythm consists of premature beats or so-called extrasystoles. These may occur at frequent or infrequent intervals and may arise in the auricles, the ventricles, or the auriculoventricular node and the junctional tissue below it. They occur much more often in the entire absence of organic heart disease than in association with it but are far from rare in individuals who have valvular or heart muscle damage with or without evidence of impaired myocardial reserve. Regardless of their point of origin, premature beats are characterized by a disturbance of heart rhythm in which, at intervals, a heart beat occurs before its expected time. The degree of prematurity of the beat may be slight or marked,

and those beats which follow the preceding normal beat at a very short interval often fail to cause a pulsation in the peripheral arteries. When each normal systole is followed by a premature beat (bigeminal rhythm), a high degree of prematurity may result in a radial pulse rate which is one-half of the ventricular rate.

The clinical recognition of premature beats is seldom difficult although without mechanical aid it is not always possible to distinguish between those of auricular and those of ventricular origin. Nodal premature beats can be identified as such only in the electrocardiogram. In all varieties which complicate an otherwise normal rhythm, it is possible to detect the basic regular rhythm of the heart by careful auscultation, and the differentiation of premature beats from other types of arrhythmias such as auricular fibrillation depends fundamentally upon the ability of the examiner to appreciate that a basic regular rhythm is present but is being disturbed, usually by a single beat, at regular or irregular, frequent or infrequent intervals. In the periods between the premature beats, the normal rhythm of the heart is present. Premature beats often can be diminished in numbers or even abolished by exercise sufficient to increase the heart rate, and this response is also of help at times in differential diagnosis.

With few exceptions, a premature beat is separated from the succeeding normal heart beat by an interval of abnormal length which is known as the compensatory pause. In the case of ventricular or nodal premature beats, this pause is completely compensatory so that the interval between the normal beat which preceded the extrasystole and the first normal ventricular contraction after the premature beat is exactly equal to the length of two normal cardiac cycles. In auricular premature beats, on the other hand, the compensatory pause is of shorter duration or incomplete. When the patient's heart rate is not elevated, it is often possible to estimate the completeness or incompleteness of the compensatory pause by careful auscultation and in this way form a reasonably accurate opinion as to whether the premature beats are of auricular or ventricular origin.

Auricular Fibrillation

Auricular fibrillation may occur in young individuals with perfectly normal hearts but usually is due to rheumatic heart disease (particularly with mitral stenosis), coronary sclerosis, hypertensive heart disease or thyrotoxicosis. It may also occur as a complication of pneumonia and certain other febrile illnesses. In this arrhythmia there is no coordination in the contraction of the muscle fibres of the auricles so that a section of the auricular musculature at any given moment would

show fibers in all stages of contraction and relaxation. Auricular systole is abolished and the auriculoventricular node is showered with a rapid, irregular succession of impulses. Ventricular contractions occur in response to a variable number of these impulses, and a rapid, entirely irregular ventricular rhythm results. Ventricular contractions which follow the preceding response by a very brief interval often fail to cause a pulsation in the peripheral arteries, and a pulse deficit results. It is the absolute irregularity and the entire absence of an underlying basic rhythm that constitutes the pathognomonic feature of the disturbance. As long as the ventricular rate is elevated, auricular fibrillation can be recognized without difficulty, but when the rate has been reduced by means of digitalis, very careful auscultation may be required before one can be certain of the diagnosis.

At times one hears the statement that "slight fibrillation" is present. This is always erroneous, and the term should never be used. There are no degrees of auricular fibrillation; the arrhythmia either is present or it is absent. The ventricular rate may have been reduced by means of digitalis, and at the lower rate the irregularity of the ventricles may be less apparent. The auricles, however, are still fibrillating.

Auricular Flutter

Auricular flutter occurs much less commonly than auricular fibrillation. It is due to essentially the same type of auricular disturbance as auricular fibrillation but with the difference that regular auricular contractions of limited extent occur at a rate usually in the neighborhood of 300 per minute. Because a certain degree of auriculoventricular block is almost always present, the ventricular rate is slower than the auricular. In those cases in which the degree of block is constant, the ventricular rhythm is perfectly regular while in those in which the degree of block varies, an irregular rhythm is present.

When the auriculoventricular block is constant and of such a degree as to give a ventricular rate within the usual limits of normal, the presence of auricular flutter may easily be overlooked, and the arrhythmia may be discovered only when an electrocardiogram is taken because of associated organic heart disease. Occasionally, in cases of this kind, however, careful inspection of the venous pulsations in the neck may clearly reveal three or four or even more auricular pulsations to each ventricular wave. When auricular flutter is present with a regular ventricular rate of 120 to 180 beats per minute the rhythm must be differentiated from sinus tachycardia and from auricular paroxysmal tachycardia. In auricular flutter the ventricular rate remains constant within very narrow limits and is not affected appreciably by exercise. This is in contrast to the variability of the

rate in sinus tachycardia, but does not aid in distinguishing the condition from auricular paroxysmal tachycardia. Pressure upon the carotid sinus at the bifurcation of the common carotid artery may cause transient slowing of the rate in auricular flutter or may cause an abrupt standstill of the heart of variable duration followed by resumption of the original rate. The first of these responses may also be obtained in patients with sinus tachycardia but the second does not occur. In auricular paroxysmal tachycardia, pressure upon the carotid sinus either causes an abrupt reversion to normal sinus rhythm or has no effect at all.

Because of variations in the degree of auriculoventricular block the ventricular rhythm in auricular flutter may be very irregular and may at times strongly suggest auricular fibrillation. Careful auscultation usually enables one to detect an underlying dominant rhythm, however, and this distinguishes the condition from auricular fibrillation. Furthermore, pressure upon the carotid sinus in auricular fibrillation has neither of the effects upon the rate of the ventricles which occur in auricular flutter.

Auricular Paroxysmal Tachycardia

This is one of the most interesting of all the disturbances of heart rhythm. In it, an irritable focus in the auricles takes control of the cardiac mechanism and sends out contraction impulses at perfectly regular intervals, usually at a rate between 150 and 180 per minute. No auriculoventricular block is present, and the ventricular rate therefore is the same as the auricular. The condition is characterized clinically by paroxysms which develop suddenly, last for a few seconds to many days, and usually terminate abruptly. The heart rate during an attack seldom varies more than two or three beats per minute, and the disturbance occurs much more commonly in individuals who have normal hearts than in persons who have organic heart disease.

The sudden onset of a perfectly regular tachycardia in which the heart rate is not affected by rest or exercise is always suggestive of auricular paroxysmal tachycardia. Paroxysmal auricular flutter may give rise to tachycardia of similar grade and great regularity but the two conditions usually can be distinguished without difficulty. Mention already has been made of the effect of pressure on the carotid sinus in auricular flutter. In auricular paroxysmal tachycardia, pressure on the carotid sinus either has no effect at all on the heart rate or causes an abrupt resumption of the normal heart rhythm. There are a number of other procedures that often terminate the paroxysm of auricular tachycardia with the same promptness. One of the most

effective of the these is the simple act of having the patient hold a deep breath as long as he is able. Firm pressure on the eyeballs, abrupt flexion of the body at the hips and the induction of nausea or vomiting are also effective in many patients. Sudden termination of an attack of regular tachycardia by any of these measures enables one to make an unqualified diagnosis of auricular paroxysmal tachycardia.

Ventricular Paroxysmal Tachycardia

Unlike auricular paroxysmal tachycardia, tachycardia of ventricular origin is almost always the result of serious organic heart disease. As in auricular tachycardia, the paroxysms usually are sudden in onset and termination, and the ventricular rate generally is in the neighborhood of 160 to 180 beats per minute. Levine[1] has pointed out a number of characteristics of ventricular tachycardia which are of value in diagnosis. In the first place, the rhythm is seldom perfectly regular although the variation may occur only at infrequent intervals and usually can be detected only by careful auscultation. In the second place, auscultation at the apex for a considerable length of time reveals an occasional accentuation of the first heart sound which apparently is due to simultaneous contraction of the auricles and ventricles. Finally, pressure upon the carotid sinus and the other measures which may terminate an attack of auricular tachycardia have no influence on paroxysmal tachycardia of ventricular origin.

Auriculoventricular Block

Auriculoventricular block may be of any degree from slight prolongation of auriculoventricular conduction to complete dissociation of the auricles and ventricles. Simple prolongation of the conduction time between the auricles and ventricles can seldom be detected without the aid of instruments but the various grades of heart block above this often can be recognized by careful auscultation alone. Partial heart block of that degree in which a ventricular beat fails to occur at occasional intervals is characterized by a period of silence over the precordium only slightly shorter than the time of two complete cardiac cycles. This condition can be differentiated from sino-auricular block or so-called sinus arrest only by means of phlebograms or electrocardiograms, and on auscultation one must also make certain that a faint premature beat is not being overlooked in the early part of the period of silence. In 2:1 heart block a ventricular response fails to occur after every other auricular beat. The ventricular rate usually is less than 50 per minute, and it may be possible to hear the sound, usually quite faint, which results from the auricular contractions that are not followed by a ventricular systole. In complete heart block also one can often detect the

sound of the auricular beats. Here the ventricular rate is usually less than 40 beats per minute. There is one other auscultatory finding of diagnostic importance, namely, that on listening over the apex of the heart one will note an occasional accentuation or reduplication of the first heart sound due to the chance occurrence of practically simultaneous contraction in the dissociated auricles and ventricles.

Complete heart block and partial heart block with a slow ventricular rate must be distinguished from sinus bradycardia. Unless one of the above auscultatory signs of heart block are present or unless one can detect extra auricular waves on inspection of the jugular pulse, the differentiation may not be possible by physical examination alone. It is important to remember, however, that exercise and such drugs as atropine cause little or no change in the ventricular rate in complete heart block while in sinus bradycardia a distinct increase in rate usually results.

Summary

The characteristics of the various disturbances of cardiac rhythm have been so well established that it is possible to recognize all but a few of the arrhythmias without electrocardiographic aid. Premature beats, auricular fibrillation, auricular flutter, auricular paroxysmal tachycardia, ventricular paroxysmal tachycardia and complete heart block usually can be detected by careful physical examination alone, and the various grades of partial heart block often can be diagnosed or their presence at least be surmised. Electrocardiographic corroboration of the clinical diagnosis is always desirable but the electrocardiogram today is of much greater value in the detection of heart muscle damage and disturbances of intraventricular conduction than in the differentiation of the cardiac arrhythmias.

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RECURRENT RENAL LITHIASIS

CHARLES C. HIGGINS, M.D.

With the modern facilities now available, an early and accurate diagnosis of urinary calculi may be established and surgical intervention instituted before the kidney has suffered irreparable damage. However, the recurrent formation of calculi following operation constitutes a major problem in urologic surgery and, in view of the frequency with which this occurs, the operative procedure, *per se*, must be considered as but one phase in the management of patients with calculous disease.

Numerous publications have appeared in the literature concerning the experimental production of urinary calculi, the etiologic factors associated with the formation of calculi, and refinements in operative technic, but the problem of recurrence and its prevention has only recently received attention. It is essential that intensive preoperative investigation be carried out to ascertain the etiologic factors associated with the formation of the primary calculus and that correction of the underlying factors be accomplished in order to prevent and minimize the formation of recurrent calculi. To better understand the problem, the present conceptions of calculous formation must be considered.

LESION OF THE PAPILLA

In 1912 at the meeting of the American Association of Genito-Urinary Surgeons, Caulk[1] reported a case of calcareous incrustation around one of the renal papillae and the next year, he[2] presented three additional cases in which a similar pathological process was found. Dr. Opie gave the following pathological description of the papillary lesion: "The section of the papilla with the incrustation showed that the tip of the papilla was covered with a homogeneous material, which took a deep blue stain of decalcified material. The tissue of the papilla was dense and fibrous and contained very few cells. The tissue in immediate contact with this mass has undergone hyaline degeneration. In this hyaline area, as the calcified mass is approached, numerous minute calcified granules are seen. Deeper into the substance of the papilla, the tissue is loose in texture and contains numerous blood vessels. There are also occasional collections of lymphoid cells. It was thought that the condition was due to primary necrosis of the papilla with a secondary deposition of calcium phosphate." The other cases Caulk reported included one of incrustation of the upper ureter, one of incrustation of calcium phosphate on the posterior wall of the kidney pelvis, and one of incrustation of the juxtavesical ureter. The incrustations from the posterior wall of the renal pelvis were composed of calcium phosphate with traces of

calcium oxalate. At this time Caulk raised the question as to the relationship of these lesions to calculous disease.

In 1936, Randall[3] also described a lesion of the papilla which he believed to be the initiating lesion of a renal calculus. This consisted of a sub-surface deposit of calcium and he traced from this the destruction of the covering mucous membrane and a deposit thereon of two types of urinary salts; namely, calcium phosphate and calcium oxalate. He stated that these salts appeared to be direct secondary deposits upon the calcium plaque once it was denuded of its epithelial covering. Investigation regarding the relationship of this lesion to infection, infarction, and avitaminosis is now in progress.

Infection

The relationship between infection and the formation of renal calculi has been stressed for a long time. Bartlett[4] in 1895 stated that two factors were associated with the formation of kidney stones, namely: (1) infection, and (2) stagnation. Brongersma's[5] statistics infer that recurrence following operation is usually due to infection. In aseptic cases, the incidence of recurrence was 3 to 6 per cent. Where a slight infection was present, the incidence was 27 per cent and 50 per cent where the infection was pronounced. Rovsing[6] in discussing Brongersma's paper stated that 68.18 per cent of all recurrences occurred when renal infection, either primarily or secondarily, was due to a urea splitting organism. It is of significance, however, that in 15.91 per cent of the cases, recurrences developed in sterile urine.

While attention has been directed in the last few years to the property of the proteus organism to split urea with the resultant formation of carbon dioxide and ammonia, it must be recalled that Brown and Earlam[7] have stated that 40 per cent of the Staphylococcus albus and 18 per cent of the bacilli infecting the urinary tract possess similar properties. It is necessary, therefore, not only to classify the infecting organism correctly, but it should be a routine procedure to determine if the organism has urea splitting properties.

While it may be true that infection plays a major rôle in influencing the formation of recurrent calculi, in view of the fact that many recurrences develop in the presence of sterile urine, further quest of the etiological factors is required.

Focal Infection

Diligent search for foci of infection is essential. The investigations of Rosenow and Meisser[8] demonstrate the relationship between the Strep-

tococcus and calculous formation. In 1921 they reported the results of a series of experiments in which the pulps of the teeth of six dogs were inoculated with Streptococci isolated from the urine of patients who had renal lithiasis. Calculi developed in the experimental animals and the Streptococci were isolated from the urine of the animals. Foci may be present in the teeth, tonsils, prostate, cervix, and bowel, all of which require examination.

Hyperparathyroidism

Publications by Barney,[9] Chute,[10] Albright, Baird, Cape, and Bloomberg[11] and others have focused attention on the relationship between hyperparathyroidism and the formation of renal calculi. Hunter[12] in 1931, in a review of a collected series of 32 cases of osteitis fibrosa in which there was evidence of hyperparathyroidism, noted the presence of renal calculi in 10 instances. Albright and Bloomberg[13] more recently reported 23 cases of hyperparathyroidism from the Massachusetts General Hospital and 15 of these patients had renal calculi.

During the past three years, we have made it a routine practice to study the serum calcium and inorganic phosphorus levels, blood phosphatase, and the excretion of calcium in the urine of all patients with renal calculi. A roentgenogram of the pelvis and tibiae is secured in each case. In more than 375 cases we have found only one instance of hyperparathyroidism. This patient, at the time of operation, was found to have a small tumor of one of the parathyroid glands and this was removed without difficulty. In the other cases, no evidence to indicate the presence of hyperparathyroidism was noted.

Vitamin A Deficiency

The results of experimental studies demonstrating the relationship between moderate or mild degrees of vitamin A deficiency extending over a long period of time and the formation of urinary calculi have been presented in previous publications.[14] In some articles appearing in the literature, it has been stated that a searching inquiry into the dietary habits has not indicated dietary or nutritional inadequacy. This is true in many instances; however, a dietary history is misleading and, by use of the biophotometer test, we have detected evidence of vitamin A deficiency when its presence was not suspected. Likewise, an adequate amount of vitamin A may be present in the diet but it may not be utilized properly. In several cases, we have elicited a definite history of night blindness which, as is well known, is associated with a pronounced deficiency in vitamin A. This observation simulates closely our experi-

mental observations in which a pronounced deficiency of vitamin A in the diet is not permitted, but rather a mild deficiency is allowed to extend over a long period of time.

In our series of patients with calculous disease, vitamin A deficiency has been present in 68 per cent of those who had the biophotometer test. Clinical data regarding vitamin A deficiency are gradually being accumulated. Jeghers[15] has found that "In a group of medical students, 35 per cent had low photometer readings and 12 per cent had clinical manifestations of the deficiency. The chief manifestations, in the order of their frequency, were night blindness, photophobia, dry skin, dry conjunctivae, blepharitis and follicular hyperkeratosis. The factors producing the deficiency were analyzed and showed that the skipping of meals and poor choice of foods were chiefly responsible. After dietary analyses it was concluded that 4,000 international units of vitamin A daily represent the minimal requirement for a healthy adult." The reports of Jeans,[16] of the University of Iowa, indicate that moderate or mild degrees of vitamin A deficiency are more prevalent than we have been led to presume. Studies of the seasonal fluctuation of the vitamin A content of various foods such as milk, cream, butter, and eggs have been made by the Ohio Experiment Station at Wooster, Ohio. Their results indicate the difficulty of determining whether or not a patient is securing adequate amounts of vitamin A even though a careful dietary history is taken.

Stasis

Attention also has been directed toward the possible relationship between the formation of renal calculi and stasis. Stasis, as we know, has a tendency to render urine alkaline and to induce precipitation of salts in an alkaline urine. Hunner[17] has stressed the importance of ureteral stricture with resultant stasis as an etiological factor in the formation of recurrent calculi. Since the advent of intravenous urography, pre- and postoperative evidence of stasis may be noted and corrective procedures employed to eradicate the causative factor instrumental in producing it. Certainly, intravenous urography should be employed in all cases of renal calculi to ascertain if stasis is present.

Metabolic Factors

Cystinuria: Calculi composed of cystine are an unusual type of stone. The association of cystinuria and cystine lithiasis has been stressed by Seegar and Kearns.[18] In a review of 181 collected cases of cystinuria, cystine calculi were noted in 124 instances.

Gout is another metabolic condition in which an excess of crystalloids may appear in the urine, microscopic examination of the urinary sediment revealing the presence of uric acid crystals and urates. Not only may calculi composed of uric acid be produced, but the patient may experience attacks of colic as showers of uric acid crystals are passed. Gout, however, need not be present for uric acid calculi to form. The amount of uric acid eliminated daily in a normal individual varies largely according to the individual diet. Normally, 0.3 to 1.2 gm. are excreted in 24 hours.

Phosphaturia: Temporary phosphaturia may be caused by eating foods containing an excess of alkaline ash, such as large quantities of citrous fruits. Permanent infected phosphaturia is associated with the presence of an organism that has the power of splitting urea, rendering the reaction of the urine strongly alkaline and this is frequently associated with recurrent formation of calculi. Permanent noninfected phosphaturia is said to be associated with alteration in function of the large bowel.

Oxaluria: Oxaluria has been stated by Neville[19] to be associated with a deficiency of vitamin B in the diet. However, an excessive intake of food having a high oxalic acid content may be associated with elimination of more than the normal amount of oxalates in the urine with resultant oxaluria.

Xanthin calculi: Urinary calculi composed of xanthin are of rare occurrence. Kretschmer[20] in 1937 collected a series of 15 cases and added one of his own. Mathews[21] has stated that the most important purine found in the human urine is uric acid, but there are present also from 30 to 50 mg. of purine bases, xanthin, hypoxanthin, guanine, and adenine. He estimates that from 16 to 60 mg. of purine bases are eliminated in the urine daily as the purines are the end products of the metabolism of the nucleins. An excessive intake of food high in purine content may be elicited by a careful dietary history in such instances.

Trauma

Statistics have indicated that recurrences following nephrolithotomy are more frequent than when the simpler procedure of pelviolithotomy is employed. In 1915 Cabot and Crabtree[22] reviewed a series of cases at the Massachusetts General Hospital and found an incidence of 56 per cent recurrence following nephrectomy and 51 per cent following pyelotomy. Braasch and Foulds[23] in 1924 estimated a recurrence of 10.79 per cent. They stated a recurrence of 11.85 per cent followed pyelotomy and 24.03 per cent followed nephrolithotomy.

Certainly, a minimum of trauma should be inflicted during the surgical procedure. As evidence of the danger of trauma, we have seen cases in which, when a recurrent stone was carefully sectioned, a blood clot was found to be the nucleus.

Type of Stone

The removal of a branched calculus extending into the calices is more prone to be followed by a recurrence than when the stone is confined to the pelvis of the kidney itself. This may be due to injury of the calix or the infundibulum in the removal of the calculus or a small fragment of the calculus may be broken off and this acts as a nucleus for secondary formation of a calculus. It is also true that the removal of small multiple stones is followed by a recurrence far more frequently than when a small, solitary stone is removed. A small calculus may not be demonstrable on the roentgenogram and thus may be overlooked, but with a suction apparatus which we use, minute calculi have been removed on several occasions when their presence was not suspected previously.

In a similar manner, stones of a soft consistency are more prone to be followed by a recurrence, possibly because sand remains to act as a nucleus for secondary formation of a stone. Thorough lavage of the pelvis and calices after removal of a calculus eliminates this possibility.

Surgical Aspects for Prevention

As stated previously, we believe the surgical procedure which is accompanied by a minimum of trauma to the kidney is preferable. In an attempt to deliver the kidney, handling it or traumatizing the renal parenchyma by manipulating the kidney is unnecessary as a routine procedure. The operation is preferably carried down to the renal pelvis which is exposed by means of flexible retractors and the calculus is removed without delivering the kidney.

In instances in which there is no renal infection or if infection is not pronounced, the incision in the renal pelvis should be closed with fine catgut sutures passing through only the outer layers of the pelvis and not through the mucosa where it might be retained and act as a nucleus for recurrent formation of a calculus.

Joly[24] has stated that even temporary leakage of urine increases the risk of recurrence of stone and should be avoided if possible. He further states that if the kidney has been drained, it is usually found to be infected with Staphylococcus albus. Rovsing[6] also stated that urinary leakage of only a few days' duration was sufficient to infect the kidney. In cases in which a more pronounced infection is present, pelvic drain-

age may be necessary for thorough drainage and irrigation to eradicate the infection.

Nephrolithotomy is employed in cases in which pyelotomy does not seem feasible. When a calculus is confined to a calix and the infundibulum is too narrow to permit its extraction through the pelvis, a localized nephrolithotomy is employed. This procedure should, however, always be as conservative as possible. In the removal of a staghorn stone, nephrolithotomy may be necessary and I believe adequate drainage should be instituted in such cases.

A heminephrectomy may be the preferable procedure in some instances in which a calculus is confined to a dilated calix. In the presence of a stricture of the infundibulum with infection, the latter can only be eradicated by this procedure and fewer recurrences will follow this method than if a localized nephrotomy is employed. After removal of the calculus, the calices and pelvis are thoroughly lavaged with saline solution and a suction tube is placed in the calices and pelvis to remove any remaining debris.

When small calculi are being removed, a roentgenogram of the exposed kidney is advisable to locate a small calculus which might be overlooked and produce a false recurrence.

Postoperative Routine

Elimination of stasis: If the postoperative urogram which is secured in all cases reveals evidence of stasis, ureteral dilatation and lavage of the renal pelvis is advisable. I believe this is essential. At the time of dilatation, specimens of urine may be secured from the kidney for culture and determination of the pH.

Eradication of infection: As stated previously, it is extremely important not only to classify the organism but also to determine if the organism possesses urea splitting properties. We attempt to eliminate the infection if possible before the patient is dismissed from the hospital, utilizing the period of convalescence for this purpose. If the organism is of the colon group, we find now that the infection may be eradicated by mandelic acid therapy rather than the ketogenic diet which we formerly employed. We have also used mandelic acid in combination with the ketogenic diet. Mandelic acid therapy should not be employed indiscriminately and the contraindications to its use, such as impaired renal function which leads to acidosis, have been cited previously in the literature. Limitation of fluids and a careful check of the pH of the urine are essential to satisfactory results with mandelic acid.

In the presence of the group of colon bacilli that split urea with the

formation of carbon dioxide and ammonia, we have usually been able to acidify the urine by use of acidifying agents. This is in contrast to the proteus group in which I have been unable to acidify the urine by the ketogenic diet, the acid-ash diet, or acidifying agents. Obviously, if the pH of the urine cannot be shifted from the alkaline to the acid side, the acid-ash diet routine is not efficacious. Likewise, it may be impossible in this group to acidify the urine by administration of ammonium chloride. As the ammonia is synthesized in the body, urea will be broken down by the proteus organism into ammonia. It leads to blood acidosis, causing increased elimination of calcium and phosphorus in the urine which, being alkaline and at a point at which the phosphates and carbonates in the urine are precipitated, may lead to enlargement of the calculus. Individualization of the patient is obviously necessary. I have found the proteus infection extremely difficult to eradicate and the use of vaccine therapy, mandelic acid, prontosil, and other drugs have usually been followed by poor results. For treatment of the staphylococcus group, salvarsan in addition to other medication is employed. It is important to eliminate the infection if possible before the patient leaves the hospital. In this way, close supervision can be kept and then either the acid-ash or alkaline-ash diet may be started.

In view of Rosenow's and Meisser's work,[8] a careful check of foci of infection is essential and, if such are found, they should be eradicated, tonsils, teeth, prostate, cervix, and bowel being carefully studied.

Treatment of hyperparathyroidism: If clinical investigation has demonstrated the presence of hyperparathyroidism, correction is obviously necessary to prevent a recurrence. In the one case in which we have seen coexisting renal calculi and hyperparathyroidism, the patient's general condition and renal function were such that we were able to remove the adenoma of the parathyroid gland before attacking the kidney problem. Each patient must be studied carefully to ascertain which problem should receive priority in treatment.

Vitamin A deficiency: Vitamin A in large doses is administered postoperatively for two reasons: (1) to correct vitamin A deficiency if it be present and (2) for its specific effect on epithelial structures.

During the past three years, in several instances at the time I removed a calculus from the renal pelvis, I excised for pathological examination a small portion of the pelvis contiguous to the calculus. In the majority of cases, microscopic examination revealed denudation of the epithelium and ulceration extending through the mucosa. This is undoubtedly due to trauma from the calculus. The ulcerated area is frequently covered with adherent granular debris and calcific deposits which may act as a nucleus for secondary stone formation. Certainly, from this

site, colloid (fibrin) is produced which will serve to bind together whatever salts are being precipitated, dependent on the pH of the urine. Thus I believe vitamin A is of value to promote rapid healing of this ulcerated area even in cases where the biophotometer test gives normal results.

Dietary Adjustment

As stated previously, experimental evidence led us to believe that the incidence of the formation of recurrent calculi could be minimized by a carefully planned dietary regimen which would be utilized to control the pH of urine. Although it has been our observation that the majority of recurrent calculi are composed of salts which are precipitated in an alkaline urine, special attention must be directed to the cases in which the calculi are composed of cystine, uric acid, and xanthin, i. e., salts which are precipitated in an acid urine, as well as those composed of oxalates, a salt which is precipitated in a wide range of urinary reactions.

In our experience, the initial dietary control requires or at least is better managed if the patient is hospitalized, the cooperation of the Dietetic Department being essential. When the acid-ash diet is utilized, an initial diet with an excess acid-ash of 17.3 cc. is prescribed. The various constituents of the diet, i. e., the proteins, fats, and carbohydrates, are varied daily until the pH of the urine secured by catheterization of the ureters is maintained at 5.2 to 5.5. This may necessitate increasing the acid-ash content of the diet to 28 or 30 cc. and, in some cases, additional acidification by ammonium chloride may be necessary. Obviously, if the pH of the urine cannot be shifted to the acid side by the diet, as in many cases of proteus infection, satisfactory results cannot be anticipated. Ammonium chloride is administered in the form of enteric coated tablets (7½ grains). If the proteus infection cannot be eradicated, the pH of the urine in the majority of cases cannot be maintained at 5.2 to 5.4 and precipitation of the alkaline salts will continue.

In addition to the acid-ash diet, if the calculi contain traces of oxalates, it is advisable to restrict foods having a high oxalic acid content, substituting those containing little or no oxalic acid. As suggested by Snapper[25] it is well to attempt stabilization of the colloids of the urine by the administration of sodium benzoate in the group of patients who have calculi composed of oxalates, in view of the fact that these salts precipitate in a wide range of urinary reactions. At the present time, we are giving from 1 to 2 gm. sodium benzoate three times a day. As a general rule, the patients consume a sufficient amount of glycocoll that the resultant formation of hippuric acid from the benzoic acid occurs. Snapper has also recommended supplying additional glycocoll by having the patient eat every day soup extracted from calf bones. In cases

in which the calculi are composed of uric acid, the alkaline-ash diet is utilized. The basic diet then has an excess alkaline-ash of 17.3 cc., the contents of the diet being varied daily until a pH of 5.4 to 5.6 is maintained. Care must be exercised that the pH is not shifted too strongly to the alkaline side, as precipitation of phosphates and carbonates must be avoided. In this group, a purine-free or low purine content of the diet is necessary. A similar diet is utilized for calculi composed of cystine or xanthin.

It does not suffice merely to prescribe a list of foods having an excess of alkaline- or acid-ash. The diet must be prescribed as carefully as that which would be instituted for a patient with diabetes. It has been found necessary to alter the diet from time to time in order to maintain the pH at the correct level. The patient makes daily determinations of the pH and these are recorded and presented to the physician at frequent intervals. The diet may then be adjusted or the medication altered. If this is not carefully observed while the patient is under dietary management, failures are bound to ensue and beneficial results will not be obtained.

In conclusion, the management of patients with calculous disease requires intensive study, diligent observation, and a conscientious and judicious postoperative routine. Since adding our dietary program to the other procedures used postoperatively following removal of renal calculi, we have reduced the incidence of recurrence from 16.9 per cent to 4.6 per cent, recurrences having developed chiefly in the group of patients in whom the pH of the urine could not be controlled successfully. If satisfactory treatment for the proteus organisms can be attained eventually, the incidence of recurrence can be reduced to a minimum.

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PITYRIASIS ROSEA

Some Common Errors in Diagnosis with a Brief Review Stressing the Differential Diagnosis

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The national campaign against syphilis is doing much to arouse in physicians and especially in the laity a syphilis consciousness. The campaign, while it seeks to draw attention to all forms of syphilis, stresses particularly the detection and management of the highly infectious primary and secondary manifestations. Syphilis not only simulates other diseases in its late manifestations but the secondary eruption may imitate many other dermatoses. Many persons have now learned that secondary syphilis is a generalized eruption and we have been impressed during the past two years by an increasing number of persons who, on discovering the presence of pityriasis rosea on their bodies, have come to us for assurance that they do not have syphilis.

Pityriasis rosea is a harmless and clinically unimportant disease *per se*, but, although uncommon (an incidence of about 5 per 1000 skin diseases[1]), it takes a prominent place in the differential diagnosis of secondary syphilis with which it may be confused. The acute generalized maculopapular and papular types which occasionally appear on the face and genitalia at first sight do look formidable. If the busy physician makes only a superficial examination or is unfamiliar with the fundamental characteristics of the disease, he may be led to an erroneous diagnosis of syphilis. An intimation of such a diagnosis to the patient may do irreparable damage to both the patient himself and his domestic happiness as well as cause the physician much embarrassment.

The superficial, cutaneous, fungous infections occupy a position parallel with that of syphilis in relation to pityriasis rosea, due mainly to the actual increase in the incidence and the laity's increasing familiarity with tinea infections. When a patient presents himself with a lone herald plaque or the herald plaque accompanied by a few macules of the secondary eruption, it is easy to assume that they are lesions of tinea corporis. If the herald plaque occurs in the genitocrural region, there is a still greater possibility of mistaking it for tinea (eczema marginatum). The seriousness of this lies in eczematizing the skin with strong keratolytics and fungicides.

Pityriasis rosea is not often confused with psoriasis or suborrheic dermatitis as evidenced by the absence of such indications in the records of the 108 cases of pityriasis rosea seen in the past 10 years.

The following case histories are typical examples showing the results of failure to recognize pityriasis rosea:

Case 1: Eczematization of the Neck, Chest, and Axillae by Treating the Herald Plaque and First Few Macules as Ringworm.

A young woman, 30 years of age, entered the Clinic in October, 1938, complaining of an eruption on her neck, trunk, and extremities. Two weeks previously she had noticed a pink and slightly itching spot about the size of her little finger nail on the left side of her neck. After a few days the spot had increased in size and, thinking that it was a "ringworm," she went to her physician who confirmed her suspicion. A salve was prescribed which was applied three times a day. Three or four days later, other similar spots began to appear on the neck, upper part of the chest, and about the axillae. She visited her physician again, this time complaining of severe itching. He advised her to continue to apply the salve on her neck and chest and to use a lotion for the axillary regions; however, this treatment did not stop the appearance of new lesions. Because the ointment made her chest and neck inflamed, she stopped using it and a few days later she came to the Clinic. Just prior to the onset of the primary lesion, she had had a head cold and sore throat.

Examination of her skin revealed a moderately severe erythematous, vesicular dermatitis of the neck, upper chest, and axillae. The initial lesion apparently had been obliterated by the eczematization. The remainder of her trunk, the thighs, and upper arms showed a symmetrical and bilateral distribution of typical pityriasis rosea.* The general physical and laboratory examinations revealed no findings of significance. The Wassermann and Kahn tests gave negative reactions.

Case 2: Eczematization Due to Self-Treatment of Pityriasis Rosea for Ringworm.

A minister, a woman 29 years of age, came to the Clinic in October, 1938, with a history almost identical with that of the patient described in Case 1, except that the initial spot appeared on an old thyroidectomy scar. As it enlarged it became ring-like and, believing it to be a ringworm, she applied musterole ointment. This made the skin very red, inflamed, and pruritic. A month later, three days before admission, the secondary eruption appeared.

Examination of the skin revealed a healing, but scaly, erythematous dermatitis on the neck through which the initial plaque was plainly visible. The trunk, upper arms, and thighs showed typical pityriasis rosea.

The general physical and laboratory examinations gave normal findings. The blood Wassermann and Kahn tests gave negative reactions.

Case 3: Pityriasis Rosea Treated as Syphilis Producing Syphilophobia in a Case of Anxiety Neurosis.

This young man, a salesman 33 years old, came to the Clinic on January 6, 1938, complaining that a severe, itching rash on the trunk had been present for three months. The initial spot had appeared in the left groin. The first physician he consulted stated that the rash was a fungous infection and treated it with several roentgen ray treatments and a lotion. As this did not stop the spread of the eruption, he saw another physician who said that he probably had a drug eruption. He was put on a regimen including a strict diet of fruit juice, frequent catharsis, and potassium permanganate baths. The patient insisted that he lost 30 pounds in two months.

* For the sake of brevity, a description of the cutaneous lesions is omitted from the case reports. They are described in detail in the section on morphology.

Examination of the skin revealed a dry, scaling dermatitis in large patches on the trunk and upper parts of the extremities; its exact nature could not be determined because of the marked potassium permanganate discoloration of the skin. However, several plaques on the back and in the groins suggested those of pityriasis rosea.

The general physical and laboratory examinations revealed no abnormalities. The blood Wassermann and Kahn tests gave negative reactions.

Following treatment with soothing lotions and ointments plus two fractional doses of superficial roentgen rays, the dermatitis cleared up.

The patient was not seen again until six months later when he stated that he felt fairly good except that a burning sensation in the groins had persisted and he couldn't sleep. It was further elicited that because of this he went to see a psychiatrist who told him that he had an anxiety neurosis, which diagnosis has been confirmed. At this examination the examiner noticed a dry skin with keratosis pilaris and a general enlargement of the superficial lymph glands. More searching examinations were made but nothing strikingly abnormal was found. He was assured that there was nothing organically wrong and an attempt was made to correct the neurosis.

Six months later, on November 1, the patient returned to the Clinic, this time exhibiting a typical pityriasis rosea. He stated that this eruption was similar to the one that he had the previous year, and this time he was certain that there was something really wrong with him. He therefore went to a physician friend who took a blood test and gave him 10 injections of neoarsphenamine. Frequent blood tests were made but all were negative. On one of his territorial trips, he consulted a dermatologist who also took blood for testing but it gave a negative reaction. Careful questioning did not elicit a possible source of infection.

On examination the patient was seen to be very apprehensive and depressed. He was perspiring profusely and his hands showed a coarse tremor. Another general physical and neurological examination gave negative findings except for slightly enlarged inguinal lymph glands. The eruption was typical of pityriasis rosea with the herald plaque in the right groin. The nature of the eruption was explained to him and he was assured that it was not syphilis.

A week later he returned to the Clinic because of boils in the axillae. Several large, deepseated and painful nodules were present in each axillae. These have since disappeared after roentgen therapy and incision. Three weeks later the eruption had almost completely disappeared.

Since this is the time of year in which the greatest number of cases of pityriasis rosea are seen and also the time in which errors in diagnosis are commonly made, a brief review of the etiology, clinical manifestations, differential diagnosis, and treatment of this condition is considered timely.

Etiology

In recent years accruing evidence is supporting the theory that pityriasis rosea is a specific exanthem with special periods of incubation, evolution, and decline. Three etiologic factors have been proposed:

(1) Thomson and Cumings,[2] following experiments with filtered extracts of scales from the lesions and on clinical comparison with the

TABLE 1

MONTHLY INCIDENCE OF PITYRIASIS ROSEA INCLUDING 1133 CASES COLLECTED BY WEISS ET AL,[8] 156 CASES REPORTED BY THOMSON AND CUMINGS,[2] 230 CASES REPORTED BY PERCIVAL[1] (ESTIMATED FROM GRAPH), AND 108 CASES FROM THE CLEVELAND CLINIC.

Authors	*No. of Cases*	*Jan.*	*Feb.*	*March*	*April*	*May*	*June*	*July*	*Aug.*	*Sept.*	*Oct.*	*Nov.*	*Dec.*
Weiss et al	1133	111	101	108	95	117	74	51	76	102	98	96	104
Thomson and Cumings	156	13	14	15	12	10	11	9	...	14	23	19	14
Percival	230	16	23	22	6	16	12	13	20	21	24	30	28
This series	108	10	10	5	8	8	7	5	6	13	10	18	9
Total	1627	150	148	150	121	151	104	78	102	150	155	163	155

acute exanthemata, suggested that the disease was probably due to a specific virus.

(2) In 1927, Wile[3] succeeded in producing in four persons an eruption simulating that of pityriasis rosea. This was done by inoculating into the skin the fluid contents of blisters raised on the primary and secondary plaques. Benedek[4] in 1932 isolated an organism from the plaques and fluid of blisters raised on the plaques by Wile's method. With an extract from this organism (schizosaccharomyces hominis) he claims to have produced an eruption similar to that of pityriasis rosea.

(3) Some French authors[5] believe that their experimental data indicate a streptococcus as the cause.

The incubation period is reckoned from the time of onset of the herald plaque to the appearance of the secondary eruption. The average period is from 7 to 14 days with a minimum of a few days and a maximum of about two months.

Authoritative opinion is divided as to the portal of entry. The herald plaque is believed by some to be the portal of entry, while others believe the tonsils and other lymphatic structures of the throat are sites of entrance of the virus. Experimental evidence and clinical observations associating the location of the herald plaque at points of entrance such as vaccination, operative wounds, needle pricks, and most commonly on the trunk where the virus may enter the skin due to close-fitting and ill-ventilated clothing supports the former view.[6] The presence of diseased throats, inflamed tonsils, and cervical adenopathy support the latter viewpoint.

Lord[6] has collected reports of from two to four persons in the same family or in close association who acquired the disease in rapid succession at about a week apart. Percival's figures[1] suggested that by 1930 the disease in Edinburgh had reached epidemic proportions. Even though pityriasis rosea is uncommon, recurrences in the same individual are rare. These observations suggest that pityriasis rosea may be an infectious disease and that one attack establishes an immunity.

Table 1 shows the incidence of pityriasis rosea according to months. It is seen that the greatest number of cases occur in the months of fall, winter, and spring which is comparable to the maximum incidence of many acute infectious diseases and exanthemata.

The age incidence is shown in Table 2. The incidence curve reaches its maximum in the third decade of life. Many acute exanthemata and acute infectious diseases have their maximum incidence in children below 15 years of age. No satisfactory explanation for this difference has been offered.

TABLE 2

AGE INCIDENCE OF PATIENTS WITH PITYRIASIS ROSEA

Author	*Total*	*Age in Decades*					
		1–10	*11–20*	*21–30*	*31–40*	*41–50*	*51–60*
Weiss et al	379	54	91	124	74	30	6
Thomson and Cumings	156	35	49	39	24	4	5
Fowle	220	21	43	77	46	11	..
Highman	51	4	6	13	21	3	4
Fox	74	5	15	35	9	10	..
Percival	234	29	76	80	31	17	1
This series	108	4	12	42	34	10	5
Total	1223	152	292	410	239	85	21

Percival[1] gathered statistics from nine recorded series and 1112 cases elsewhere. In these he found the average sex incidence to be 57.4 per cent in women and 42.6 per cent in men. In two series, however, the ratio of males to females was 2 to 1. In our group, 67 per cent of the patients were women and 33 per cent men or approximately 2 to 1.

Symptoms and Morphology

Systemic reactions when present are almost always mild. Only a few of our patients stated that they felt fatigue or malaise. Thomson and Cumings[2] mention that a few of their patients complained of dypspepsia and mild arthralgia.

Infections of the upper respiratory tract have been reported to precede or accompany the onset of pityriasis rosea in up to 90 per cent of cases. We have found similar complaints in about 10 per cent of cases. Cervical and general lymphadenopathy occurs in a few cases.

Mild elevations of the temperature have been observed at the onset of the eruption.[7] This has not been seen in our series.

The majority of patients do not complain of pruritus. In the minority, itching may be so mild that the patient does not complain of it unless asked, but the itching may range from mild to severe. Weiss et al[8] noted pruritus in 26.8 per cent of cases while we observed it in 35 per cent of our series. The most severe pruritus occurs in the urticarial type of pityriasis rosea. If the skin has been eczematized by treatment, pruritus is usually pronounced.

According to Percival[1] the herald plaque has been observed in from 12 to 94 per cent of cases; Weiss et al[8] found it in 27 per cent, and we have noted its presence in 74 per cent of our cases. The herald plaque appears most commonly on the trunk. The neck, buttocks, thighs, upper arms, legs, forearms, and face in the order named are the next most frequent sites. It first appears as a small pink macule which in a few days usually attains the size of a quarter or larger. At this size, it often assumes an oval, ring-like form with a pale, fawn-colored center. When the lesion is grasped between the fingers, the scaly surface of the center crinkles in a manner similar to cigaret paper. At the inner edge of the border there is a scaling collarette. The border usually varies from a tawny salmon shade to pale red and is slightly elevated. The lesion is almost always the largest, most mature of the eruptions and may attain the size of the palm. The long axis of the oval lies along the lines of cleavage of the skin.

After an average of from seven to fourteen days, the plaque is followed by the secondary eruption. Klauder[9] divides the efflorescence

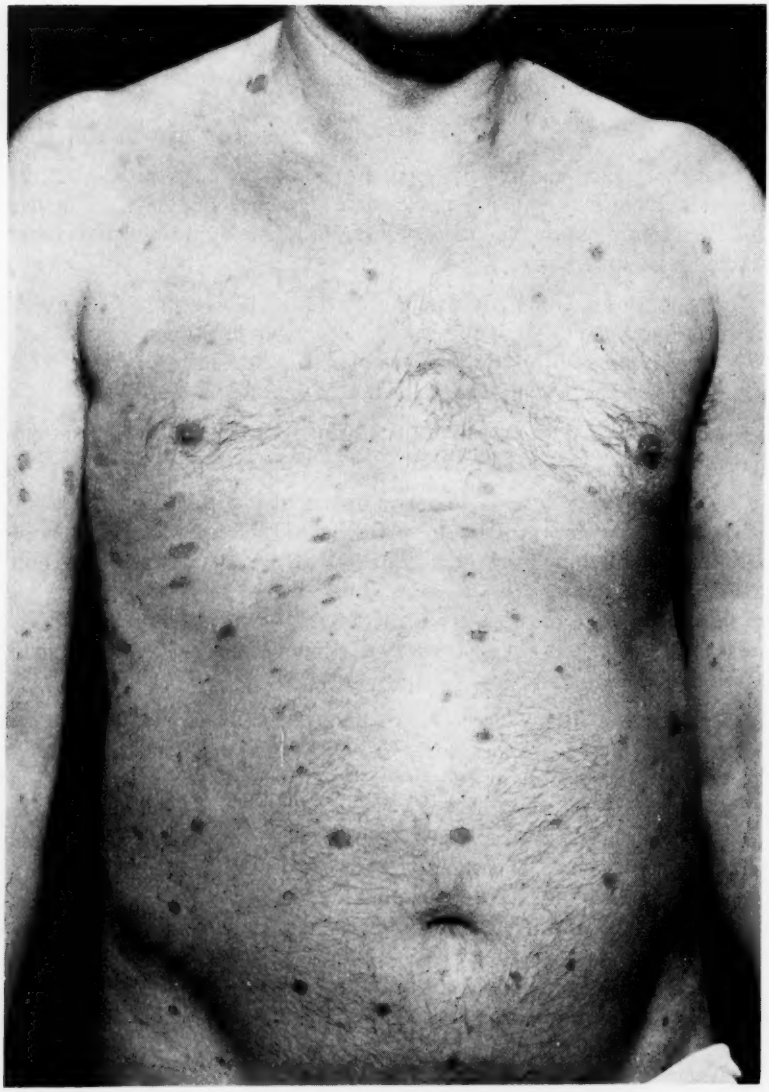

FIGURE 1: Macular type of pityriasis rosea. Note herald plaque on the neck and distribution of macular lesions with axial arrangement along lines of cleavage.

into three main types: macular, papular, and vesicular. The macular type is subdivided into punctate, guttate, nummular, circinate, and urticarial varieties. Maculopapular, follicular, and miliary types are variations of the papular group.

Urticarial and vesicular types are rare. In the former, the lesions are wheal-like and itch intensely but after a few days they tend to assume the characteristics of typical patches. Vesicles may be seen in the latter form. In the very rare instances when lesions occur on the palms or soles they are usually vesicular.

The macular type (Figs. 1 and 2) is the most common manifestation.[9] A particular case may be classified as a subvariety depending on which type of lesion predominates. The macules are discrete or confluent; in the latter event scaly, erythematous patches are formed which may be irregular in outline. If the clearing of the patches is complete, circles are formed constituting pityriasis circinata. Circinate lesions are not likely to be seen when the eruption is of recent duration. The macular and circinate lesions usually duplicate the morphology of the herald plaque, and may enlarge to a diameter of two or more inches. The clearing centers, ovoid shape, and long axes along the lines of cleavage are important diagnostic features.

In the less common papular type, the maculopapular variety occurs most frequently. The papular variety consists of well-defined, but not grouped papules; they are rosy pink in color, varying in size from a pea to a dime, and are scaly from the onset. Macules may coexist with the papules thus constituting the maculopapular variety. In negroes a combination of follicular papules, papules, and macules is more frequently observed than in white persons.

The distribution of the eruption in a typical case is limited mainly to the trunk. The lesions are most numerous about the axillae and sides of the thorax and flanks. A lesser number are found on the neck, upper arms, and thighs. There may be a few on the forearms and legs, but they are rarely found on the face, hands, and feet. In children and infants, the eruption may be profuse on the face and scalp.

Pityriasis rosea may be restricted to certain areas such as only one side of the body, genitocrural, upper chest, and axillary regions, or the face and neck. In inverted pityriasis rosea, the lesions are limited to the extremities. When the exanthem is limited to the genitocrural and axillary regions, there may be some difficulty in differentiating it from ringworm (Fig. 3).

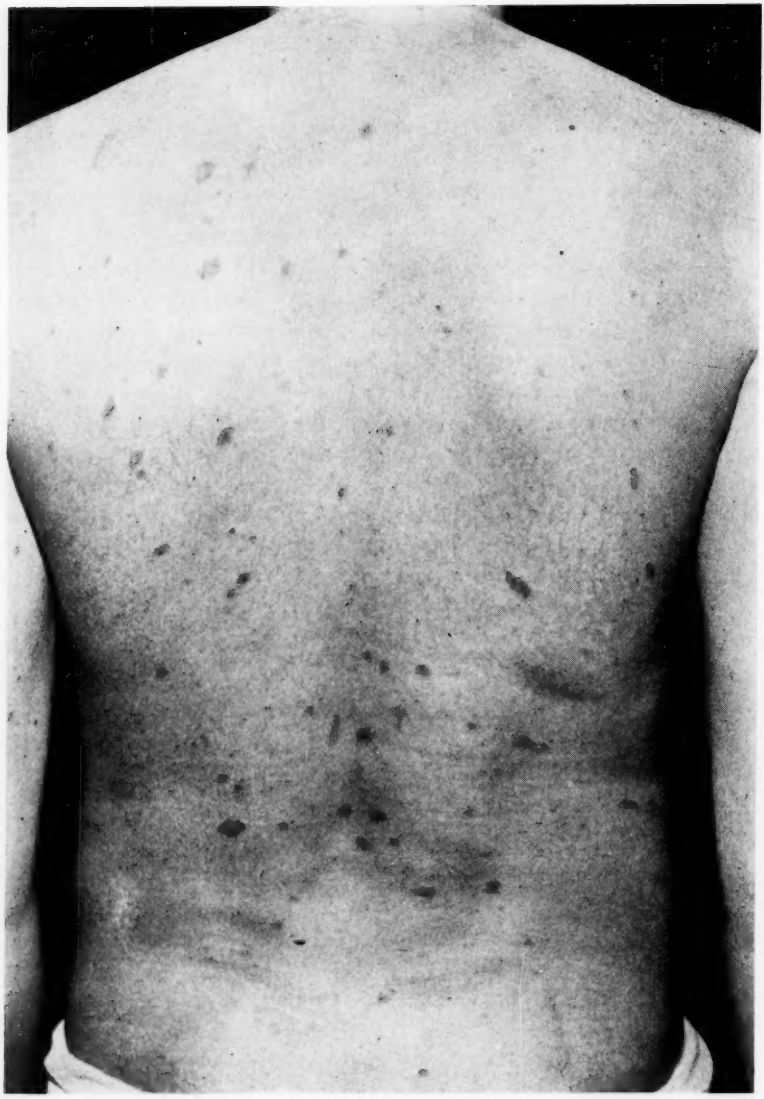

FIGURE 2: Macular lesions on the back. Same case as Fig. 1.

Diagnosis

The diagnosis of pityriasis rosea is based on the following features: (1) The history of onset of the herald patch preceding the secondary eruption and the presence of the plaque itself; (2) the crinkled, cigaret paper-like scaly surface of the macules; (3) the arrangement of the macules, circinate lesions, and even papules with their long axes along the lines of cleavage; (4) the distribution of the eruption which chiefly involves the trunk.

The differential diagnosis between pityriasis rosea and the secondary eruption of syphilis probably is best shown in tabular form (Tables 3, 4 and 5).

Table 3

DIFFERENTIAL DIAGNOSIS OF PITYRIASIS ROSEA AND SECONDARY SYPHILIS

Macular and Circinate Pityriasis Rosea	*Macular Syphilid*
1. History and finding herald plaque	1. No herald plaque
2. No chancre	2. Chancre present in 90 per cent of males, smaller percentage in females
3. Positive Wassermann and Kahn reactions in small percentage—almost always coincidental	3. Wassermann and Kahn reactions positive in almost 100 per cent
4. Presence of oval, fawn-colored lesions with central cigaret paper-like crinkled scaling	4. Macular syphilids not scaly, dull pink to red or brownish red color
5. Slight infiltration if any	5. More infiltrated
6. Long axes along lines of cleavage	6. May be slight suggestion in roseolar syphilid
7. Mouth lesions very rare.	7. Mucous patches in mouth and anus common. Spirochetes frequently found
8. Confluence with retiform arrangement when eruption is profuse	8. Macules and papules remain discrete
9. Lesions on face, hands, feet, palms, and soles very rare	9. Face, palms, and soles are common sites
10. Constitutional symptoms mild and general glandular enlargement very uncommon	10. Constitutional symptoms may be marked and general glandular enlargement common

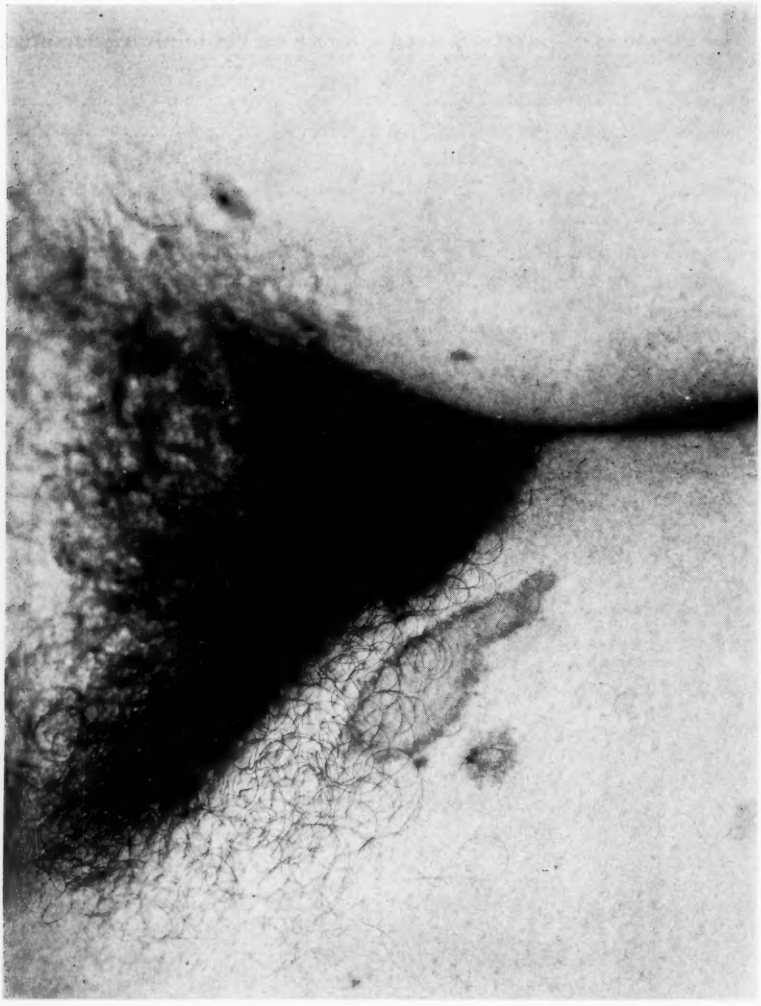

FIGURE 3: Herald plaque of pityriasis rosea. Compare with figure 4.

All the patients in our series had routine laboratory examinations including blood Wassermann and Kahn tests. Of the series only four patients had syphilis, two of whom had late syphilis and pityriasis rosea developed during anti-syphilitic treatment. In the third case which was being treated for acute syphilis, the eruption occurred during the week following the last injection of the first course of neoarsphena-

TABLE 4

DIFFERENTIAL DIAGNOSIS OF PITYRIASIS ROSEA AND SECONDARY SYPHILIS

Papular Pityriasis Rosea	*Papular Syphilis*
1. Papules discrete and rosy-pink, superficial and noninfiltrated	1. Discrete, deeper shades of red to brownish red, shotty, and infiltrated
2. Confluent in axillary and genitocrural regions but no condylomatous formation	2. Remain discrete but lesions about genitals and anus often become condylomatous
3. Seldom on face, hands, and feet	3. Common on face, palms, and soles
4. Other characteristics listed in table 3	4. Other characteristics listed in table 3

TABLE 5

DIFFERENTIAL DIAGNOSIS OF PITYRIASIS ROSEA AND SECONDARY SYPHILIS

Circinate Pityriasis Rosea	*Annular Syphilid*
1. Lesions large circinate; when become confluent, form gyrate patterns	1. Usually discrete but may form gyrate patterns
2. Superficial, slightly elevated and infiltrated; tawny salmon colored border	2. Elevated, firm, infiltrated borders of dull red to brownish red color
3. Crinkled cigaret paper-like scaling	3. Surface of lesions usually smooth but may have slight scale
4. Other characteristics in table 3	4. Other characteristics in table 3

mine, five weeks after all signs of the syphilitic secondary eruption had disappeared. The fourth patient gave a history of having had a chancre five years before and also gave positive reactions to the Wassermann and Kahn tests. In all four cases, the eruption was typical.

Ringworm: Table 6 shows the important points in differential diagnosis of pityriasis rosea and ringworm.

Seborrheic dermatitis: The scaly, macular type of seborrheic dermatitis may simulate pityriasis rosea. However, in most cases there is a history of slow evolution and chronicity of seborrheic lesions in the seborrheic areas such as the scalp, behind the ears, on the forehead,

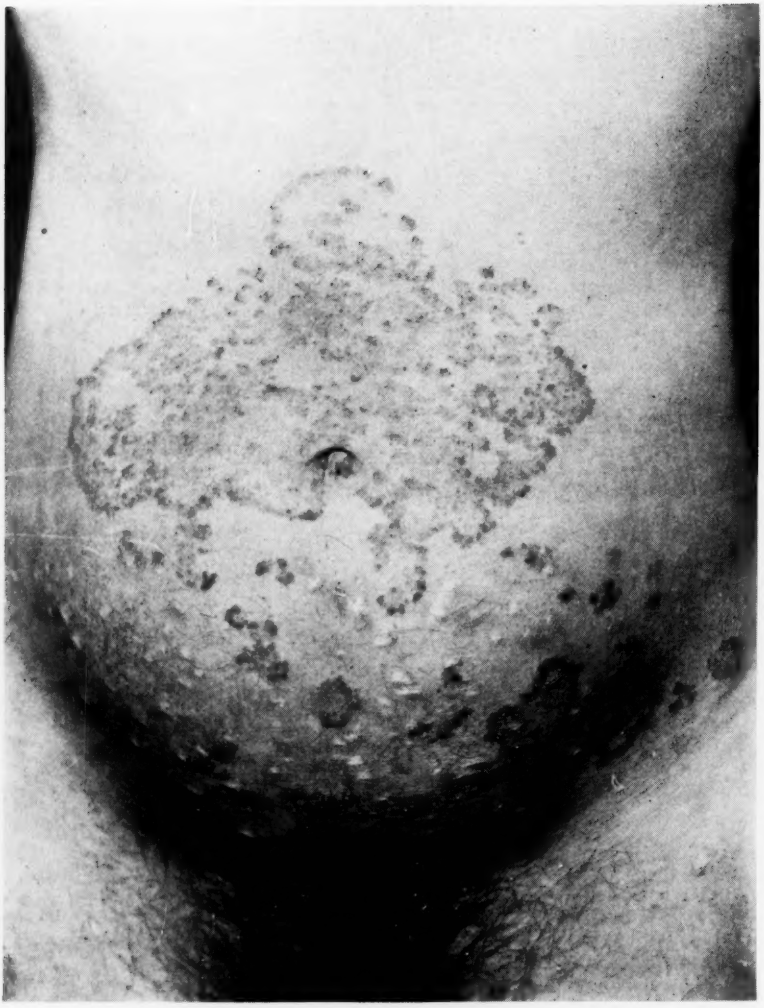

FIGURE 4: Disseminated tinea corporis. Scales showed many fungous hyphae. Note sharp, serpiginous, vesicular border of large lesion on abdomen, and new lesions within the larger ones. Compare with figures 1, 2, and 3.

base of the nose, midportion of the chest and interscapular region. Erythematous patches are likely to be in the axillae or beneath the breasts of women. The lesions have a characteristic yellowish pink color with more abundant, coarser, and greasy scales. In contrast the four characteristics listed above for the diagnosis of pityriasis rosea

TABLE 6

DIFFERENTIAL DIAGNOSIS OF PITYRIASIS ROSEA AND RINGWORM

Herald Plaque and Macular Pityriasis Rosea	*Ringworm of Body (Tinea Corporis and Cruris)*
1. Herald plaque most common on trunk, oval, long axis along lines of cleavage, no vesiculation	1. Most common on face, neck and hands, and genitocrural region, brighter red, circular lesions with raised vesicular border; no axial arrangement
2. No peripheral or satellite lesions	2. Peripheral vesiculopapules common
3. Fawn colored, dry central crinkled cigaret paper-like scale	3. Scale more thick and tenacious in center. On border when removed fluid escapes
4. No hyphae of fungus growth seen in scales	4. Fungus hyphae practically always found in scales
SECONDARY ERUPTION	
5. Rapid evolution to maximum number of lesions in few days to a week	5. Slow evolution over period of weeks or months with peripheral spreading to form large gyrate and serpiginous patterns. Usually few lesions (Fig. 4)
6. Usually bilateral and symmetrical	6. Usually asymmetrical, rarely bilateral
7. Oval patches with axial arrangement	7. Circular. May be concentric rings. No axial arrangement

should be kept in mind in the differentiation between it and seborrheic dematitis.

Psoriasis: Psoriasis usually is a chronic affection lasting over a period of years, while pityriasis rosea is acute and of short duration. The lesions of psoriasis are red, more inflammatory, and covered with laminated, silvery white scales which, when removed by scraping, expose minute bleeding points. The sites of predilection are the scalp and extensor surfaces of the elbows and knees.

Psoriasis may be initiated by an acute onset or the chronic stage may present at times an acute exacerbation. The lesions, although brighter red and with fewer scales, are usually punctate, guttate, or circular without axial arrangement. When the scales are scraped off these lesions, bleeding points may be seen. An acute attack may come and go as such, but usually it terminates in a chronic form of the disease. This never occurs in pityriasis rosea.

Drug eruptions: Dermatitis medicamentosa due to arsenicals and bismuth very rarely simulates pityriasis rosea.[10] The resemblance is superficial and differentiation is of little practical importance to the internist or general practitioner.

Treatment

Because pityriasis rosea is a mild, acute exanthem of short duration with practically no complications, treatment is unnecessary in many cases. In those patients who have a mild infection of the upper respiratory tract or systemic reaction, symptomatic treatment may be instituted.

If pruritus is a pronounced feature, mild sedatives may be given for a few days. Locally, a lotion consisting of phenol 1 to 2 per cent, resorcin 2 to 3 per cent, zinc carbonate 10 gm., zinc oxide 10 gm., olive oil 64 cc. and aqua calcis, q.s.a.d. 128 cc. may be employed as an antipruritic and to remove the scales. The eruption appears to produce an increased irritability of most patients' skin such that stronger keratolytics may cause a secondary dermatitis. It is for this reason that the skin of most patients is eczematized when strong keratolytic and fungicidal ointments and lotions are used.

When it is necessary to shorten the course of the disease for cosmetic reasons, we employ ultraviolet irradiation which in most cases gives good results. The skin is irradiated for one minute at a distance of 30 inches the first dose. Thereafter the daily treatment is increased by one minute to 15 minutes, at which time the distance is shortened by one inch daily until the irradiation is 15 minutes at 18 inches distance. Usually the eruption will begin to disappear in about 2 weeks.

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TESTICULAR DEFICIENCY DUE TO HYPOTHYROIDISM

Report of a Case

E. P. McCullagh, M. D.

The following case is presented to show the relationship of excreted androgens to various symptoms, including impotence, and because it appears to illustrate a relationship between hypothyroidism and the excretion of androgenic materials. The urinary androgens in all probability reflect fairly accurately the degree of hypogonadism which is present.

History: A white man, 50 years of age, was examined first in June, 1936. He complained of gradually increasing impotence and loss of sexual libido over a period of 18 months. There had been no infections of the genito-urinary tract in the immediate past or previously, no orchitis, and no severe general infections. His symptoms apparently could not be ascribed to exhaustion, since they had not improved following vacations and adequate rest. For six months impotence had been almost complete and no ejaculations had occurred under any circumstances. Energy and endurance were fairly good. He tended to be rather irritable, but otherwise there were no nervous symptoms and none suggestive of hypothyroidism.

The physical examination revealed an alert, healthy-looking man whose height was 73 inches and weight 166 pounds. His temperature was normal. The pulse rate ranged between 65 and 80 beats per minute. His skin was very slightly dry, although the color of the skin and the mucous membranes was good. He had a slight gingivitis. The blood pressure was 115 systolic and 80 diastolic. The prostatic secretion contained from 10 to 20 white blood cells per high power field and appeared normal. The prostate and the genitalia were apparently entirely normal. No other findings that seemed to have a bearing on the symptoms were noted.

Laboratory Tests: Urinalysis showed an occasional white blood cell and a faint trace of albumin. The red blood cells numbered 4,950,000, the level of hemoglobin was 97 per cent (Haden-Hauser), and the white blood cells numbered 8,900 with 75 per cent neutrophils, and 25 per cent lymphocytes. The level of the blood urea was 24 mg. per 100 cc. The level of the blood sugar was 98 mg. and of the blood creatinine 0.9 mg. per 100 cc. five hours postprandial. The blood Wassermann and Kahn tests gave negative reactions. A modified Friedman test which was done in May, 1936, showed a frankly positive test with four plus fresh corpora lutea in the test animals. A second Friedman test in October, 1936, gave entirely negative findings. An assay for

urinary androgens was made on April 28, 1936, by the chloroform extraction method.[1] This showed no comb growth in two birds tested. This test was repeated on May 15 and August 3, 1936; on each of these occasions the two birds tested showed 4, 2, 3, and 4 mm. comb growth respectively. By this method the normal average is about 10 mm. of comb growth. Roentgen examination of the sella turcica revealed no abnormalities.

Diagnosis: It appeared to us at that time that we were dealing with a case of functional hypogonadism since there were distinctly low androgen assays by the method used and these were associated on one occasion with an excess of urinary prolan. This was considered evidence of pituitary hyperfunction and was in keeping with the belief that hypogonadism was present.

Treatment and Progress: In June, 1936, treatment was begun with the administration of testosterone in oil*, each 1 cc. of oil containing 2.5 mg. of active material. Injections of 1 cc. were continued at the rate of about three times per week between June 10 and November 6. On this dose a little improvement was noted, although it was not striking —on July 21 erections appeared during the night for the first time in three or four months but no other change was noted. In August no further improvement had occurred. The patient complained somewhat of tiredness, but no other symptoms suggestive of hypometabolism were detected. In August, 1936, basal metabolic rates were found to average minus 32 per cent. One month later urinary androgens measured by a slight modification of the method of Koch[2,3], utilizing benzol extraction and five white leghorn capons as test objects, showed 3 international units of androgenic substance. This was at the time 2.5 mg. of testosterone were being given three times per week. This assay was repeated twice in October and showed 5.0 and 1.0 international units in the 24 hour specimens. Twenty-four hour specimens of urine from normal young men contain between 20 and 100 units by this method. In November, 1936, a modified Friedman test was again found to give a positive reaction, urinary androgens had risen to 39 units, and there was a slight decrease in symptoms.

On December 17, 1936, the basal metabolic rate was minus 25 per cent and on December 19 treatment was changed to testosterone propionate, 5 mg. being given three times per week. Within a few days there was a distinct increase in potence. This treatment was continued until February 3, 1937, with the exception of two weeks ending November 22. A specimen of semen was examined on February 2, 1937. The volume was 1.2 cc.; the total number of spermatozoa present was

* The androgens used in the treatment of this patient were Schering's Oreton made available through the courtesy of Dr. Erwin Schwenk, Dr. Max Gilbert, and the Schering Corporation.

1,920,000; the motility of sperms was very slight. Study of stained smears indicated that about 20 per cent were morphologically abnormal. A single dose of 25 mg. of testosterone propionate was given on February 3 and 24 hour specimens of urine collected on February 3, 4, 5, 6, and 8 showed 65, 35, 20, 9, and 26 international units respectively. On February 9, the dosage of testosterone propionate was increased to 10 mg. three times per week and the impotence almost completely disappeared. This treatment was continued until June, 1937. The patient was seen again on May 27, 1937, at which time the basal metabolic rate was found to be minus 15 per cent. Injections were omitted for six weeks and it was found that 10 international units of androgens were being excreted. Within the month following discontinuance of androgen therapy he had noticed considerable exhaustion, he was somewhat dull mentally, the nails were rather brittle, and there was some paresthesia of the hands and feet. He had had relatively little impotence for nearly six weeks after discontinuing the injections, after which this symptom had returned. On May 27, 1937, desiccated thyroid was prescribed in a dose of 1 grain per day. The fatigue, mental dullness, and paresthesia disappeared promptly. The impotence disappeared almost completely and as much following the use of thyroid alone as it did on the injections of testosterone propionate.

In September, 1937, the basal metabolic rate was minus 23 per cent, androgen excretion had increased to 45 international units, the dose of desiccated thyroid was increased to 3 grains per day and in October, 1937, the basal metabolic rates averaged minus 5 per cent. The patient was almost entirely free from symptoms.

Comment

In this case the presenting symptom was sexual impotence. At first, a diagnosis of testicular deficiency was made on the basis of repeatedly low assays for urinary androgens associated with an excess of urinary prolan. Although the basal metabolic rate was decidedly depressed, there were no clinical symptoms which were highly suggestive of hypothyroidism and this diagnosis was postponed. Injections of testosterone propionate relieved the impotence when the dosage was adequate to raise urinary androgens to a range within normal. Discontinuance of treatment was followed by a fall in urinary androgens to low levels and recurrent impotence. Subsequently, distinct clinical evidence of hypothyroidism appeared and following treatment with desiccated thyroid alone, more marked clinical improvement was obtained with thyroid therapy only than was seen following treatment with androgens. This improvement was associated with a significant

rise in the level of the urinary androgens and a disappearance of impotence.

In the course of treatment the rate of excretion of androgens following the injection of testosterone propionate was tested. It appears from repeated assays that 25 mg. of testosterone propionate was excreted in three days. This provides a suggestion as to the frequency with which such injections should be made. The rise in androgen excretion on the fifth day following this injection suggests that the androgen production was depressed temporarily by this injection since normal individuals have been shown to respond in a similar manner following such treatment.

In conclusion it appears that in this case hypothyroidism caused impotence by the production of a secondary testicular deficiency.

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TWO YEAR RESULTS OF THE TREATMENT OF ESSENTIAL HYPERTENSION BY CELIAC GANGLIONECTOMY

GEORGE CRILE, M.D.

In the treatment of essential hypertension we have performed 476 operations on the adrenal sympathetic system in 285 patients. These have included 325 celiac ganglionectomies in 199 patients. In the latter series 35 patients were operated upon two or more years ago. From the study of the results in these 35 cases we have drawn certain conclusions as to the indications for operation.

The calendar age has no effect upon the results of celiac ganglionectomy. It is the physiological, not the calendar age, that counts. What happens to the blood pressure as a patient grows older? It tends to rise secondary to advancing sclerosis. That progressive increase in the blood pressure cannot be cured, that is, there is a cardiovascular age, and that age may be established in younger individuals for there is a certain stage in hypertension in which there is an irreversible condition due to sclerosis alone. Wherever there is molecular injury and repair, as in scars and burns, which are subjected to pressure or irritation, the scar grows. By the same process when there is a certain amount of scar tissue or sclerosis in the vascular tree it will grow, just as does a scar in the esophagus, in the intestines, or a scar from a burn at the elbow. Such scars grow larger because of continuous molecular injury and repair.

In a case in which sclerosis is present the blood pressure may fall after celiac ganglionectomy, but the extent to which it will fall is limited by the cardiovascular age of the patient. Existing sclerosis cannot be taken out any more than old age can be cured. We have had one child of nine years whose physiological age was ninety years as judged by the degree of sclerosis in his blood vessels. The blood pressure of this child was 220/140. The calendar age, therefore, has nothing to do with the indications for operation. From our experience we have become able to judge how much sclerosis can be present and not prevent good results from the operation.

I have been astonished at the large number of young people who have this disease. Not only do they have the disease but a goodly number of them have passed the period of any possible help.

Among our older patients operated upon more than two years ago was a surgeon sixty-five years of age with malignant hypertension. His blood pressure has been reduced from 220/110 to 165/95. He now has no heart consciousness. His improvement has been so great that he is now quite active, whereas before his operation he was unable to

do anything at all. He suffered from frightful headaches and dyspnea —from all the symptoms that accompany malignant hypertension. All these symptoms have disappeared.

An exceedingly significant fact is that the celiac ganglion in this case weighed 4000 milligrams, whereas the normal ganglion weighs from 250 to 350 milligrams or less.

In our cases of essential hypertension, all the ganglia have been found to be much larger than the ganglia in such diseases as hyperthyroidism and neurocirculatory asthenia. At first I thought this large size was due to a hypertrophy, but we couldn't conceive how that could occur in nerve tissue—and then we considered that in people like this surgeon, who is a very forceful person, in people who are active, in highly strung individuals, this mechanism is not enlarged—as the thyroid gland is enlarged in exophthalmic goiter—but rather, that the large celiac ganglion is peculiar to people of this type, that there are families which have a common characteristic, and that characteristic is that they have the power to do much work, they are tireless people due to the possession of a large celiac ganglion.

Other similar cases might be cited but this one is sufficient to show that the calendar age has nothing to do with the indications for operation. Our sixty-five year old surgeon is better off than some patients who were only in their twenties. Everything depends upon the physiological age and the degree of sclerosis in the vessels. Some of our very good results are in patients in the sixties, but not in patients with senile sclerosis.

If a patient has had a cerebral accident, is he then a suitable candidate for celiac ganglionectomy?

We have had a patient who had such an accident and who was operated upon over two years ago with an excellent result. For quite a long time we did not recommend any operation for any patient who had had a cerebral accident until a patient came along who had made a very good recovery from his hemiplegia, had a very clear mind, and was young, and I thought we should give him a chance. I find that the indications for operations are still present after a cerebral accident, provided only that there is no deterioration of the brain. If there is deterioration of the brain cells there is no more reason for believing that the operation would be successful than for believing that we could return to the patient a sound and an active brain, than for believing we could return a senile brain to its earlier status. We never consider operation after a cerebral accident excepting in those patients who still have a quite normal cerebral activity and who with respect to certain other standards present no contraindications to the operation.

Is celiac ganglionectomy indicated in the presence of nephritis? If the hypertension is secondary to glomerulonephritis, operation is of course contraindicated. On the other hand, if the nephritis is secondary to the hypertension and the urea clearance remains above 50, celiac ganglionectomy may be performed.

Is celiac ganglionectomy effective in the malignant phase of hypertension? Many of our patients, including the elderly patient whose case has been described have had malignant hypertension as indicated by the ocular findings, even advanced malignant hypertension, and the edema of the discs has disappeared after the operation together with the other symptoms. Sight that is lost is not restored, but the edema disappears.

Among the thirty-five patients operated upon two years or more ago ten have died at varying periods after they left the hospital. One of these died from uremia, the other nine from cerebral hemorrhage.

It is generally accepted that approximately 60 per cent of patients with essential hypertension die from cardiac disease. According to this percentage six of these ten patients would have died from heart disease if they had not been operated upon, but there was not one cardiac death. Moreover, in our whole group of patients there has not been a single cardiac death in the hospital following the operation.

It should be borne in mind that the heart is an integral part of the dynamics of the circulation of the blood and that it is controlled by the sympathetic system just as are the blood vessels throughout the arterial tree. It should follow that the heart and the coronary artery should be protected by celiac ganglionectomy. That the heart is directly affected by the operation is indicated not only by the fact that none of our patients has died from heart disease, but also by the fact that following celiac ganglionectomy the patients have been relieved of the cardiac symptoms—of heart consciousness and coronary pain.

Advanced age, the duration of the disease, the presence of the malignant phase of the disease, the presence of coronary disease, the presence of nephritis secondary to the hypertension provided that the urea clearance can be controlled—none of these is a contraindication to operation.

What is the effect of celiac ganglionectomy upon the blood pressure?

In the series of thirty-five patients that we are considering the average decrease in the blood pressure has been 39/20. The extent of the decrease is indicated by the following table:

Pressure Reduced	*Systolic*	*Diastolic*
20 points or more	78.6%	57.1%
30 " " "	57%	35.7%
40 " " "	42.9%	14.3%
50 " " "	21.4%	7.1%—60 points
75 "	7.1%	

Syptomatic improvement was registered in 91 per cent of these thirty-five patients. Precordial pain was relieved in 83 per cent. Eighty-one per cent have returned to their regular occupations.

In the long run the value of any surgical procedure and medical measure is told by the patient himself. If the patient is able to return to his former occupation, if he is relieved of his subjective symptoms, then that determines, and that only, the value of operation.

CLINICAL ASPECTS OF HYPOTHYROIDISM

C. L. Hartsock, M.D.

The secretion of the thyroid gland must be maintained at a fairly constant level of production if the human organism is to remain in a state of well-being. For a number of reasons, some known and some unknown, many individuals are unable to maintain an adequate production of thyroxin and this results in various states of disability. The degree of thyroid insufficiency and the age and rapidity of onset are variable factors which serve to produce so wide a range of clinical pictures simulating other conditions that frequently the primary source is not readily apparent.

To suspect the presence of hypothyroidism is all that is necessary to make a correct diagnosis and eventually entirely relieve all the symptoms that result from such a deficiency. However, because of the remarkably negative and unimpressive character of most of the signs and symptoms of hypothyroidism, this condition frequently escapes detection. In view of this peculiar lack of identifying characteristics and the failure of this disease to be impressive in nature, it seems justifiable to present a subject that offers no new features, purely with the object of keeping before you the possibility of a much overlooked cause of many morbid conditions.

The following simple classification will serve as an outline for the further discussion of the problem.

1. Myxedema—severe hypothyroidism of adults.
2. Cretinism—severe hypothyroidism of children.
3. Postoperative or postradiation hypothyroidism and hypothyroidism due to exhaustion of the thyroid by untreated hyperthyroidism. Patients in whom this latter condition occurs may show symptoms of both hypothyroidism and hyperthyroidism so that the condition is frequently called "dysthyroidism."
4. Incipient hypothyroidism—mild and atypical cases in patients of any age.

Myxedema

The most obvious physical sign of severe hypothyroidism in adults is a characteristic thickening of the skin, especially of the face, eyelids, and the supraclavicular region of the neck. This swelling or edema formerly was thought to be due to deposits of mucin in the tissue, and for this reason the term "myxedema" was introduced and still continues to designate the clinical picture which results from marked diminution of thyroid function in adults. Following the introduction of methods for the measurement of the metabolic rate, it was found that in many

cases in which low metabolism was due to thyroid deficiency, this characteristic condition of the skin was very slight or was completely absent. For this reason it is better to confine the term "myxedema" to the classical syndrome in which a group of other characteritic signs and symptoms is practically always present and to use another term to describe those cases in which this sign is absent, especially as cases in the latter group show such marked variations in the clinical picture that they are all too frequently overlooked. It is better to describe such cases under the separate classification of *incipient hypothyroidism*. I realize that these two types apparently differ only in degree and that many of the incipient cases, if unrecognized, would go on to the myxedematous stage. It is for this very reason that I consider it advisable to present the clinical picture of the premyxedematous stage more definitely, in order that these cases may be recognized earlier. The early cases are more likely to be overlooked than is any other definite clinical entity and this is due in part to the unfortunate choice of the word *myxedema* to describe a condition in which the symptom which gives it its name does not appear in the early stages. When myxedema is present the thyroid deficiency is marked and frequently of long standing. The onset of symptoms has often been so gradual that the patient has been entirely unconscious of the fact that his health has been far from normal; consequently, he does not consult a doctor until the beginning of rather marked mental changes.

In the advanced stage of the disease the patient may complain of almost any symptom which can result from low metabolism. A summary of the literature discloses that symptoms referable to every organ in the body have been attributed to thyroid deficiency and have been relieved by the administration of thyroid extract. It is obviously impossible, therefore, to describe all the symptoms which may be present in myxedema so I shall discuss only those signs and symptoms which are generally present. In the section on incipient hypothyroidism I shall describe the more unusual signs which, of course, may also be present in cases of true myxedema.

Patients with myxedema present a characteristic appearance of the face which should practically always be considered as diagnostic. The features are coarse, the eyes are puffy, the hair is dry and coarse, and frequently very sparse. The speech may be slow, and the patient gives the impression of slow cerebration, the memory being especially poor for recent happenings. If left alone for a short time the patient may fall asleep. The mood is usually quiet and placid but melancholia and depression with marked anxiety may be present.

The patient is always physically tired and frequently complains of soreness and stiffness in the muscles and joints. In spite of being over-

weight these patients suffer from the cold and require heavy clothing and heavy bed covering. Digestive symptoms are common; constipation is practically always present.

Physical examination reveals a low temperature, a dry skin which feels thick and edematous, especially in the face, hands, feet, and supraclavicular fossae. The nails are brittle and ridged. The pulse is slow and the blood pressure is low, the pulse pressure being especially low. Albumin is frequently present in the urine and there is nearly always some anemia which occasionally is marked enough to suggest pernicious anemia. Free hydrochloric acid often is absent.

Cretinism

Cretinism is the term applied to the marked retardation of physical and mental development produced in children by severe thyroid deficiency. This condition is frequently congenital and the retardation of development begins at birth, but rarely, except in the most marked cases, is it discovered until the child is found to be slow in the development of activities and of normal functions, such as teething, talking, and walking. Even then, recognition of the condition is often delayed because the characteristic appearance usually does not develop clearly until about the second year. It is then noted that the growth is stunted as the result of a general disturbance of the nutrition of the osseous system. The skin is rough and dry. The hair is coarse, often giving the appearance of tow. The features are bloated. The tongue is thick and protrudes, giving a beastlike expression in very severe cases. The teeth appear very slowly and are prone to decay. The bridge of the nose is low and in typical cases the entire picture is unmistakable. In milder cases cretinism must be differentiated from rickets, birth injury, mongolianism, dwarfism, and achondroplasia. Careful study will easily differentiate these conditions but, except for rickets, it is better to treat any of them with thyroid extract until the diagnosis is definitely determined, than to leave a case of cretinism untreated. The results of the deficiency during the period of rapid growth are permanent so that the earlier cretinism is treated, the more nearly will the patient approach the normal. In these cases treatment is often very inadequate even though the condition is recognized early. I believe it is advisable to administer thyroid extract to the point of toxicity in order to determine the appropriate dosage.

Cretinism is not common in the goiter districts in North America but sporadic cases do occur with sufficient frequency to indicate the necessity for vigilance on the part of physicians and especially of pediatricians in order that this condition may be recognized early. Moreover, in goiter districts there are very large numbers of children whose physical

and mental condition is retarded by a low grade cretinism which is not pronounced enough to produce the characteristic symptoms. These cases are similar to cases of incipient hypothyroidism without myxedema. The prophylactic treatment of goiter by the administration of iodine to children and to expectant mothers should greatly lessen the incidence of this condition. Better standards for determining the basal metabolic rate in juveniles also would give a great impetus toward the correction of these mild insufficiencies of the thyroid gland in children.

In severe cases of cretinism, the prognosis is poor on account of the marked retardation which usually has occurred before the condition is recognized by the physician. The remarkable physical changes which do occur even after a short period in patients subjected to adequate treatment are almost unbelievable.

Postoperative Hypothyroidism

Every patient who has previously had hyperthyroidism, but who after spontaneous cure, operative intervention, radiation therapy, or any other form of treatment, should be suspected of having hypothyroidism, if at any time following the changed state he again complains of ill health.

Hypothyroidism that follows in the wake of hyperthyroidism fundamentally does not differ from the spontaneous type except that it has always appeared to me to present a somewhat more bizarre picture that seems best explained by the adjustment of the organism to the rapidly varying states of metabolism. For example, it is very misleading when exophthalmos persists from a previous hyperthyroidism but in other ways the patient presents many signs of myxedema.

The chief difficulty with patients of this type is their reticence to take adequate and prolonged treatment because of their fear of bringing back their original disease.

Incipient Hypothyroidism

Cretinism, myxedema, and postoperative hypothyroidism are of relatively rare occurrence compared to the milder degrees of the disease. Incipient hypothyroidism is by far the most prevalent and most difficult to recognize of all the types. If one keeps a mental picture of myxedema before him as a guide to the diagnosis of hypothyroidism, he will entirely overlook 75 per cent of the patients who have very mild symptoms of great variation but who require specific thyroid substance for the relief of these symptoms. In its mildest states, the hypometabolism tends to exert a selective action on only one or possibly several of the organs and systems. In other words, no constant group of signs and symptoms are present. Some of the more common ones in

the various systems will be presented briefly and if these are kept in mind and associated with thyroid deficiency the incipient case of hypothyroidism can be easily diagnosed.

Central Nervous System: Somnolence is a symptom of severe thyroid insufficiency and when it is present the patient is usually in a myxedematous condition. Forgetfulness, lack of concentration, and a tendency to procrastinate are also symptoms which appear in the late stages of the disease. Restlessness, nervousness, and insomnia are more common in the mild cases. Chronic headache which recurs frequently is also a common symptom. These early symptoms are more the result of the general fatigue and hypotension than the direct results of the metabolic disturbance.

Ocular System: Muscle errors which are due to fatigue of the ocular muscles are very common and these, in turn, may cause a host of vague secondary symptoms such as dizziness, headache, neuralgia, and many others that we frequently ascribe to neurasthenia. Exophoria which occurs toward the end of the day is the most frequent type of muscle imbalance.

Ear, Nose, and Throat: A slight edema of the membranes of the nose and throat may be secondary to hypothyroidism. Allergy, another cause for boggy membranes, usually is more pronounced when it is associated with hypothyroidism. We have observed a very interesting symptom complex which is a result of this edematous condition of the membranes. When the membranes near the orifice of the eustachian tube are swollen, there is a tendency for the tube to close and the patient complains of the very annoying sensation in the ear which results from this closure. Rather typical of this type of closure of the tube is its tendency to occur and disappear, sometimes several times in the same day. The use of ephedrine and air inflation of the tube gives only temporary relief, but adequate treatment with thyroid gives quick and permanent relief. Tinnitus is sometimes due to the same cause. Degeneration of the eighth nerve should be suspected of being due to a thyroid disorder. Swelling of the tongue and chronic hoarseness are late symptoms of myxedema.

Cardiovascular System: Bradycardia should always suggest the presence of hypothyroidism but the pulse rate is an unreliable guide because in many cases it is normal or increased. Thyroid insufficiency is occasionally the sole explanation for myocardial weakness. A clue to this etiological factor is found in the low amplitude of the electrocardiographic tracing. Due to the increased cholesterol content of the blood in the presence of hypothyroidism, it may also be a factor in the production of arteriosclerosis, but no improvement is noted following

treatment with thyroid, although in early cases it is possible that the progress might be arrested.

Dyspnea is entirely a secondary symptom, but that very peculiar type of dyspnea which is best described as sighing respiration is occasionally due to hypothyroidism; more frequently, however, it is due to an anxiety state.

Gastro-Intestinal System: Obstinate constipation as a result of an atonic colon is a characteristic symptom, but all types of indigestion due to fatigue of the gastro-intestinal tract may be caused or aggravated by hypothyroidism. I observed one very interesting case of sudden periodic vomiting in a young woman. No other explanation for her symptoms was ever found and because of other distinct signs of hypothyroidism and a very low basal metabolic rate, she was treated solely from this angle with complete relief from the vomiting. The explanation for this is not clear.

Achlorhydria seems to occur somewhat more frequently in hypothyroidism but this is such a common finding in patients past middle age that coincidence would lessen the value of such statistics. Adequate therapy certainly does not cause a return of the hydrochloric acid.

Genito-Urinary System: One of the classical errors in diagnosis is mistaking a case of myxedema for nephritis because of large amounts of albumin in the urine. I observed such a case recently. The patient's symptoms had been present for twelve years and she had been consulting doctors almost continuously up until five years before our examination. At that time, her physicians made a diagnosis of nephritis, gave up all hope for her cure, and sent her home from the hospital to die. The patient ceased all medical aid or advice and peculiarly enough, her condition improved, but it was still the most advanced case of myxedema I ever saw. The basal metabolic rate was minus 41 per cent. Improvement on thyroid medication was, of course, startling.

Impotence and sterility both in the male and female should cause one to suspect hypothyroidism. In one case a woman was unable to carry pregnancies to full term, but after the institution of thyroid therapy, she had two full-term, normal pregnancies.

Glandular System: Polyglandular disturbances associated with hypothyroidism as a minor or secondary feature are very commonly found, but in many cases the entire glandular syndrome is improved by the use of thyroid therapy alone, and this is especially true in ovarian types of menstrual disorders. Great advances have been made in specific glandular substitution therapy but thyroid therapy still remains the

most potent and specific. It is of great value in the treatment of pituitary, thyroid, and ovarian types of polyglandular disorders in conjunction with other indicated hormonal therapy.

Skeletal and Muscular System: Vague muscular aches and pains frequently have their origin in thyroid deficiency. Any tendency toward degenerative arthritis is hastened by a low metabolic state. The disturbance of skeletal growth is well exemplified in the cretin.

Hematopoietic System: A mild hypochromic anemia without any other satisfactory explanation should excite a suspicion of thyroid insufficiency. The marked anemias which were thought to be due to myxedema and which simulate pernicious anemia probably also have some deficiency of the extrinsic or intrinsic factor of pernicious anemia.

Hair, Nails, and Skin: Dryness of the hair and skin, brittle and thick, coarse nails, falling hair, and premature greying of the hair are very suggestive symptoms of this disease and sometimes give the earliest clues.

General Symptoms: Obesity, both generalized and that localized around the pelvic and shoulder regions, is the classical sign which usually directs attention to hypothyroidism; however, a fact which is not so generally known is that many thin individuals who never could gain weight begin to do so immediately when they follow well-regulated and observed treatment for mild thyroid insufficiency.

Localized and circumscribed swellings are frequently of myxedematous origin. Swelling of the extremities with changes of temperature or prolonged dependency suggest an early myxedema.

Intolerance of cold and a subnormal temperature is usually found, but several cases of chronic pyrexia have been reported that responded to no therapy other than thyroid. Lack of thirst and hypohidrosis are further suggestive general symptoms.

Many other vague symptoms could be cited that are secondary to the chronic fatigue, decreased cellular function, and inadequate oxidation of thyroid insufficiency, but this would only serve to make the picture confusing. If the more important symptoms mentioned above are kept in mind, one or more will stand out prominently enough to cause the condition to be suspected and recognized.

The variation in the picture of hypothyroidism in patients in the different age groups—children, young adults, and mature adults—is also confusing. Severe hypothyroidism in the child causes the typical cretinism which presents such a classical picture and has been described. Very little is known, however, about mild degrees of hypothydroidism in children. The difficulty of obtaining satisfactory metabolic studies,

the normal variability of children's weight, growth, development, and intelligence, and the fear of using thyroid preparations in the growing child have presented many obstacles to the investigation of this problem. Undoubtedly, many of the subnormal conditions of childhood about which the mother is much more concerned than the physician eventually will be shown to be due to thyroid deficiency. Diagnostic criteria are still so limited in this group that we must wait for further studies before we can attempt to recognize and treat the incipient states of hypothyroidism in children.

Severe hypothyroidism can be present in middle-aged patients with surprisingly few of the classical symptoms. It is in this group that the more bizarre symptoms of thyroid insufficiency which were mentioned previously are seen. Patients in the older group usually present at least a few of the symptoms suggestive of the clinical picture of myxedema; rarely do they show all of them.

Differential Diagnosis: The symptomatology of the clinical syndrome, achlorhydric anemia or idiopathic hypochromic anemia, frequently suggests hypothyroidism and, unless laboratory studies clearly differentiate the two, it is sometimes necessary to determine whether iron or thyroid replacement therapy is the more specific before the true diagnosis can be determined. Some cases are apparently a combination of both conditions and these do better when both medications are used.

Any asthenic state may be confused with the hypothyroid state until a therapeutic trial proves or disproves the relation of the asthenia to a deficiency of thyroid. Only by a therapeutic trial can many such conditions be differentiated. There is, however, one very common clinical syndrome that is mistaken most frequently for hypothyroidism. I refer to the depressed emotional states that are described under various terms such as melancholia, nervous exhaustion, manic depressive-cyclothymia, involutional melancholia, cerebral arteriosclerosis, and many others. In such depressed states many symptoms are very suggestive of hypometabolism and hypometabolism is present; usually the basal metabolic rate is from minus 15 to minus 30 per cent but it is not due to thyroid insufficiency and does not respond to thyroid medication. The lowered basal metabolic rate is probably the result of the depressed function of the entire body, secondary to the depressed emotional state. Even if thyroid is administered to the point of causing symptoms of toxemia the basal rate, curiously enough, still remains low. One should be alert to sense the emotional tone of the patient and be extremely careful to avoid overstimulating the depressed patient with thyroid extract. It is in this type of patient that I have seen the very few harmful effects of the use of thyroid extract.

Obesity more than any other sign is suggestive of hypothyroidism and, owing to the difficulties of calculating accurate basal metabolic rates, some types of obesities are falsely treated for hypothyroidism.

Other than obesity and the depressed mental states, the errors of diagnosis are usually sins of omission rather than sins of commission.

Treatment

The greatest handicap to the proper treatment of thyroid deficiency is a widespread fear of the use of thyroid medication. It is true that symptoms of hyperthyroidism can quickly be induced in a patient with excessive doses of thyroid substance but they quickly subside when the medication is withdrawn. If a patient is observed frequently until a maintained dose is established, there need be no fear in the use of this drug. The best method is to gradually increase the dose of thyroid until mild symptoms of toxemia are produced, and then establish the maintenance dose at a level just below this where there were no such symptoms.

The treatment of hypothryroidism of any type consists merely in the substitution of thyroid extract for the deficient secretion. Any form of prepared gland or the active principle, thyroxin, may be used. The gland extracts are satisfactory but the products of the manufacturing companies vary greatly in their relative potency. One should select one or two extracts and become familiar with the results that may be expected from each and then be sure that the patient uses the one that is prescribed. Only in this way can satisfactory results be obtained. One should also be familiar with the action of thyroxin, for some patients in whom gland extracts are ineffective respond to this, and at times the reverse is true.

No matter how mild or severe the case, I prefer to begin with small doses and to increase the dosage gradually until the replacement is sufficient to bring the metabolism to normal, although many prefer to start immediately with doses sufficient to restore the patient to normal, this dosage being calculated on the basis of the metabolic rate. There are two criticisms of this method. First, the patient will not always tolerate large doses immediately and in consequence becomes frightened. These individuals are often familiar with the warnings in regard to the use of thyroid extract for reducing so that any untoward symptoms may dissuade them from giving any further trial to this medication. Patients who have previously had hyperthyroidism are also fearful of a return of their former trouble and must be handled cautiously. The second criticism is that any method of calculation is unreliable. Some patients with a very low metabolic rate will become normal following

dosage with very small amounts of thyroid extract and others whose basal metabolic rate is only slightly below normal will tolerate large doses.

A very important point in the treatment of hypothyroidism, which for some reason is almost universally disregarded, is that the patient should continue to receive maintenance doses after the metabolic rate has reached the normal level. Very frequently I have seen patients in whom marvelous results followed thyroid medication but who have been advised to discontinue medication completely for awhile. It seems to be the opinion that the thyroid function is restored to normal by the thyroid extract while, in truth, it is only a substitution for a deficiency which will probably continue as long as the patient lives.

I have found that there is a seasonal variation in the amount of thyroid extract required, a larger amount being required in cold weather. Patients who travel should be warned that it may be necessary to vary the dosage with their geographical location. It seems to be especially true that distinctly less amounts are necessary when patients sojourn for any length of time along the seashore. Whether or not it has any beneficial effects, I advise the use of as much fresh sea food as possible, but usually do not prescribe iodine together with thyroid extract. Early in the course of treatment, a determination of the basal metabolic rate should be made every month until the normal level is reached and the proper maintenance dosage determined. A check of the patient's pulse and inquiry concerning the symptoms of palpitation, tremor, and insomnia are made weekly to check overdosage. A very good point to remember is that it is well to administer the thyroid extract early in the day and to avoid giving it late in the afternoon or in the evening. If thyroid extract has been taken as recently as five or six hours before bedtime, even when the metabolism is well below normal, very unpleasant palpitation is often experienced when the patient assumes the recumbent position. In any case one commonly finds that the subnormal symptoms are more pronounced in the morning and, therefore, the dose should be given at this time. I do not think it makes much difference whether it is taken on a full or an empty stomach or whether it is given in enteric coated capsules.

I have mentioned the therapeutic test in doubtful cases, that is, the administration of small doses of thyroid extract for short periods. This can do no harm if the patient is carefully observed and it will often yield brilliant diagnostic and therapeutic results in an otherwise puzzling case.

THE ENDOCRINE ASPECTS OF HYPERTENSION

R. H. McDonald, M. D.

It is generally accepted that an increase in blood pressure is merely a symptom and not a disease. The use of the diagnostic term, essential hypertension, is simply a compromise with our ignorance of the etiology of the condition, the outstanding symptom being used for its designation.

A number of clinical conditions have been shown to be associated with an increased intravascular tension. One group of cases of hypertension owe their genesis to primary parenchymatous, nonsuppurative renal changes, the group commonly designated as Bright's disease. The exact manner in which hypertension develops from renal change is still a matter of debate. Recent researches by Goldblatt[1] would suggest that some interference with renal circulation produces a pressor substance which circulates in the blood stream and produces directly a contraction of the arterial musculature. Amyloid disease of the kidneys and suppurative diseases such as pyelonephritis, even apparently unilateral, may result in a marked increase in the blood pressure. The renal degeneration associated with the toxemia of late pregnancy may result in sudden and marked elevation of blood pressure. Hypertension may also be found in congenital polycystic disease and it often accompanies obstructions to the outflow of urine in such conditions as hypertrophy of the prostate gland. In these latter mechanical conditions, the onset of increased pressure may be sudden and, on relief of obstruction, it may subside as quickly as it occurred.

In the hypertension due to cardiovascular conditions, the increased pressure can apparently be explained on a purely mechanical basis. Here it represents an effort on the part of the organism to preserve circulation, especially cerebral circulation, under the pressure of circumstances which tend to lower it dangerously. In this group, the systolic blood pressure usually shows the elevation, the diastolic frequently being below normal. Thus an increased systolic pressure is common in aortic insufficiency, coarctation of the aorta, arteriovenous aneurism, and heart block.

Elevated blood pressure associated with increased intracranial pressure is well known and is seen in any space-filling lesion of the cranium as well as in asphyxia and in certain psychic states.

The increased amount of study and interest which, in recent years, has been given endocrinology has revealed a number of instances where obvious endocrinological dysfunction has been found to be associated with disturbances of blood pressure, and it seems to be a well-established fact that the physical status of the blood pressure can be varied

greatly by the endocrine mechanism. The purpose of this paper is to review briefly the evidence which has been advanced in regard to this relationship. It must be acknowledged that the data to be presented are fragmentary and proceed to no definite conclusions. Apart from the groups which have been cited, there still remains a great number of cases of so-called idiopathic hypertension in which no obvious etiological factor can be demonstrated and in which the genesis of the symptom is still a matter of controversy and conjecture. The question as to whether these have some, so far unrecognized, endocrine basis must remain unanswered at present.

The time-honored theory of the etiology of essential hypertension is that of an increased peripheral resistance attendant upon vasoconstriction, chiefly of the arterioles, thus presenting some degree of obstruction in the path of the circulation of the blood. Vasoconstriction has been shown to be dependent upon the integrity of certain fibers of the sympathetic nervous system, the stimulation proceeding from a center in the medulla. These vasoconstrictor nerves exert a tonic action on the vessels; this may increase or decrease under various circumstances and is abolished by section of the nerves. In addition, it is stated that there are vasodilator nerves which also are of sympathetic origin according to some authorities, while others state that these are of parasympathetic origin. Less is known of these and they have not as yet acquired any practical importance. Stimulation of the sympathetic nerves results in the production of sympathin in the muscle cells. This material has an action similar to adrenalin; it is absorbed into the blood stream and may produce effects in other parts of the body, its effect on the vascular musculature being to produce powerful tonic contractions. Parasympathetic stimulation, on the other hand, has been shown to produce acetylcholine or parasympathin which is depressant in its action. It has not been shown, however, that the blood, spinal fluid, or urine of human beings with hypertension invariably contains a pressor substance. Recent work by Goldblatt[1] and Prinzmetal and Wilson[2] minimizes vasomotor activity as a factor in hypertension and ascribes the increased peripheral resistance to an intrinsic vascular hypertonus, presumably of humoral origin from the kidney.

Concerning centers above the medulla which may exert a control over this mechanism, Sir Humphrey Rolleston[3] suggests that the nuclei of the posterior part of the hypothalamus control the sympathetic division of the autonomic nervous system, whereas those in the anterior portion are the seat of the parasympathetics. Lesions of the hypothalamus are known to be associated with polyuria, glycosuria, and probably obesity, but no evidence has apparently been produced to show that they have

any effect on blood pressure. Physiologically, at least, this regulation of circulation by the vasomotor nerves is supplemented by the action of substances circulating in the blood, the most certain instance of this being when the internal secretion of the adrenal gland is released in circumstances of general vasoconstriction. The influence of the nerves and the chemical substance exercise a joint control over vascular tone.

The control of the nervous mechanism of circulation by the hypothalamus is very closely allied to the function of the adjoining pituitary gland. Heretofore greater etiologic significance in hypertension has been ascribed to pituitary disturbances than to the effect of these disturbances on the hypothalamus. Recently, however, the conception seems to have changed somewhat. Now it is considered that changes in the pituitary may influence the nuclei of the hypothalamus either directly or mechanically through pressure or the effect of irritation or secondarily through transfer of pituitary secretion by the hypo-physio-portal system of vessels in the case of secretion of the anterior lobe, or through the tissue spaces of the pars nervosa to enter the third ventricle through its wall in the case of the secretion of the pars intermedia. In addition to the influence of the pituitary secretions upon the hypothalamic vegetative centers, there seems good evidence that the centers themselves exert an influence upon the pituitary as well as other endocrine glands, the so-called central neuro-humoral mechanism of Roussy and Mosinger[4].

Anterior lobe of the pituitary gland: In considering the anterior lobe of the pituitary from the physiological point of view, it has not been suggested, so far as the writer is aware, that any vasopressor hormone exists, although enough function has been ascribed to that particular organ to give it an undisputed title as the body's busiest bit of tissue. Yet, only thirty years ago such eminent physiologists as Schäfer and Herring[5] referred to the anterior lobe of the pituitary as having no physiological effect and in the same year Salmon[6] suggested that the secretion of the pituitary gland caused sleep. It seems possible that increased pressure might be expected from excessive administration of the adrenotropic hormone.

Posterior lobe of the pituitary gland: It was shown as early as 1895 by Oliver and Schäfer[7] that the intravenous injection of an aqueous emulsion of whole pituitary produced a rise of blood pressure, arterial constriction, and increased force of heart beat, and in 1898 Howell[8] proved this pressor effect to be due to the secretion of the posterior lobe. Schäfer and Swale Vincent[9] confirmed Howell's results but noticed that a second injection produced a fall in blood pressure. These workers then described a depressor substance in the posterior lobe which differed from the pressor substance in that it was soluble in absolute alcohol and

ether. Generally, it is assumed that the intramuscular injection of pituitrin into the human subject is followed by an increase in blood pressure, but numerous investigators have observed that there are no constant or striking results. In 1928 Kamm[10] and others isolated from the posterior lobe two fractions, pitressin, the pressor fraction and oxytocin which has a specific action on unstriated muscle tissue. In addition to the pressor effect, the pitressin fraction also exerts a diuretic-antidiuretic effect, and it has been suggested that an excess of antidiuretic hormone may be responsible for water retention, edema, and increased blood pressure associated with diminished urinary excretion, instances of which have been recognized clinically.

Cushing's[11] idea is, or was in 1933, that it is inconceivable that the neural core of the posterior lobe could independently elaborate a hormone. He felt that it must arise from the epithelial investment and that the active principal must come from the infiltrating basophilic cells of the investing pars intermedia which become transformed into hyaline bodies and migrate in the loose neural spaces of the posterior lobe.

Hyperpituitarism: Certain clinical conditions in which hypertension is associated with definite pituitary disease or dysfunction are of considerable interest. Acromegaly, which is usually due to an adenoma of the acidophilic cells and is, therefore, to be regarded as hyperpituitarism, frequently is accompanied by hypertension although this is exceedingly variable. Increase in intracranial pressure must, of course, be thought of as a mechanical factor in the case of a tumor of any size. Cushing's syndrome or pituitary basophilism was originally associated by Cushing with the presence of a basophilic adenoma, but later it was shown to be associated with basophilic hyperplasia without a demonstrable adenoma. Hypertension is a constant finding in this condition and may be of the malignant type. A similar clinical picture has been recorded from carcinoma, adenoma, and hyperplasia of the adrenal cortex, and in some instances somewhat similar clinical manifestations have been associated with malignant tumors of the thymus and possibly arrhenoblastomas of the ovary. Whether the basis be adrenal or pituitary, these patients present the common findings of a marked elevation of both systolic and diastolic pressures along with the painful obesity, hypertrichosis, diabetes, muscular weakness, and skeletal and sexual changes which are characteristic. Cushing ascribes this to an excessive secretion of vasopressin by the basophilic cells of the pars intermedia which have invaded the pars nervosa. Kraus[12] and Berblinger[13] described an increase in the number of basophilic cells in all cases of persistent hypertension and Russell, Evans, and Crooke[14] found a close correlation between basophilic adenoma, obesity, and

hypertension without basophilic invasion of the posterior hypophysis. Fishberg[15] points out that the symptoms of Cushing's syndrome are rare in essential hypertension and refuses to accept any suggestion that essential hypertension is of pituitary origin.

Hypopituitarism: The negative evidence derived from the study of cases of hypopituitarism is of some interest. In pituitary infantilism or dwarfism, low blood pressure is the common finding as might probably be expected from the infantile state of these patients. In Simmond's disease, which is generally regarded as being due to primary destruction of the anterior lobe or to the loss of the anterior lobe and adjacent tubercinereum, low blood pressure is the invariable rule and this is associated with the extreme wasting, low metabolism, muscular weakness, and precocious senility which these patients present. In Fröhlich's syndrome there appears to be primarily a deficiency of the gonadotropic hormone. No characteristic changes in the blood pressure are found.

In summary, there seems no reasonable evidence that the pituitary is associated with essential hypertension as it exists clinically. Hoyle[16] in 1933 found no excess of pituitrin in the cerebrospinal fluid in 189 cases of essential hypertension which he examined. However, in certain pathological states of hyperpituitarism, notably Cushing's syndrome, there appears to be a hypertension indistinguishable in its essential features from idiopathic essential hypertension, and in corresponding states characterized by lack of pituitary substance, notably Simmond's disease, low blood pressure is the rule.

Thyroid: There appears to be an amazing variation of opinion regarding the effect of hyperthyroidism on the arterial blood pressure. The usual opinion is that there is a moderate rise in systolic blood presture with a diastolic pressure either normal or more commonly below normal so that increased pulse pressure results. Goodall and Rogers[17] in 1920 expressed the opinion that there were three phases of hyperthyroidism as far as the question of blood pressure is concerned: first, a short, primary hypertension due to the vasoconstriction caused by an output of adrenalin following emotion; second, the stage of low blood pressure lasting for years due to dilatation caused by thyroid secretion; third, a late stage of hypertension due to secondary changes in the cardiovascular system and reduction in thyroid activity. These observers regarded the systolic pressure as usually less than normal, the pulse pressure smaller, and the diurnal variation exaggerated. Alvarez and Zimmermann[18] found the systolic pressure raised in hyper- and hypothyroidism and believed that it was due to the primary disturbances which damage the thyroid rather than to the quantity of thyroxin.

Essential hypertension has at times been regarded as the sequel of

thyrotoxicosis, and Fishberg[15] believes that it is more common in middle-aged patients who suffer or have suffered from toxic goiter than in the remainder of the population, but he feels that this is due more to a constitutional proneness to hypertension than to the thyrotoxicosis directly. Parkinson and Hoyle[19] in 1934 described thyrotoxic hypertension as being common in women over 40 years of age, frequently when a small adenomatous goiter was present, usually associated with a low diastolic pressure, and often complicated by paroxysmal auricular fibrillation; certainly, numerous cases which would fit this description have been seen clinically.

Adrenal gland: The presence of a pressor hormone in the adrenal medulla was demonstrated in 1894 by Oliver and Schäfer[7] and the presence of adrenalin in the adrenal veins was established. It has been regarded that constant secretion of adrenalin has been responsible for a vascular tonus which has had to do with the maintenance of normal pressure. Cannon[20] in 1914 propounded the view of intermittent or emergency function of the adrenal medulla in response to various types of stimulation but he has since admitted that there may well be a continuous secretion as well. Stewart and Rogoff[21] have minimized the physiological effects of the adrenal, even denying any pressor action, rather regarding it as of no importance in the maintenance of normal blood pressure.

The adrenal cortex has been the subject of much theorizing but little is definitely known regarding its function. Its association and interrelationship with other glands, particularly the pituitary, thyroid, and gonads, has been apparent. Swingle and Pfiffner[22] believe that the cortex maintains the volume of the circulating blood and that, in adrenalectomized animals, death is due to shock. Reduction of sodium, and to a lesser extent of chloride in the blood, has been regularly noticed in cortical deficiency and may play some part in the hypotension noted in adrenal failure. In Addison's disease the initial lesion is in the medulla but the syndrome is no longer regarded as due solely to a lack of adrenalin; opinion now has swung around to the idea that cortical damage is chiefly responsible for the symptoms. This change of opinion is due partially to the knowledge that physiologically the cortex is essential for life, whereas the medulla can be destroyed without causing death. The benefits derived clinically from the administration of cortical extracts supports the belief that Addison's disease is hypocortical adrenalism. However, the cortical extract, despite its clinical benefit and production of increase in muscular power, does not raise the blood pressure. It has been shown that, in adrenal cortical deficiency, there is a scarcity of basophil cells in the anterior lobe of the pituitary and

Crooke and Russell[14] believe that the hypotension in Addison's disease is primarily due to cortical deficiency and directly due to the diminution of basophil cells. At any rate, Addison's disease is characterized by a persistent hypotension together with constitutional weakness, gastro-intestinal symptoms, and pigmentation.

Tumors of the adrenal medulla—those composed of chromaffin tissue, adrenalin-secreting tissue, the so-called paragangliomas, or pheochromocytomas—have been shown to be associated with paroxysmal elevations of systolic pressure, the diastolic pressure usually remaining normal. The absence of a raised diastolic pressure differentiates this from the considerable fluctuations which may occur in essential hypertension. In this connection one must remember the crises of paroxysmal hypertension which may accompany lead poisoning with colic, eclampsia, or in irritation of the fifth cranial nerve, the vagus, and the splanchnic. The intermittent hypertension has been explained on a basis of a pathological equivalent of Cannon's emergency hypothesis. A transient hyperadrenalinemia has been the usual explanation although pressure exerted by the tumor on the abdominal sympathetics has been suggested. Crises of hypertension may, of course, occur in the ordinary patient with permanent high blood pressure and it is possible that these paroxysmal attacks are merely the forerunner of a later permanent condition.

Adrenal-cortical tumors have frequently been associated with a persistent arterial hypertension as well as with hirsutism, obesity, amenorrhea in women, and diabetes, the so-called diabetes of bearded women. It is associated also with hyperplasia of the adrenal cortex and in the cases reported from the Mayo Clinic,[23] with proliferation, adenoma or carcinoma of the adrenal cortex. The relationship of this adrenal-cortical syndrome to Cushing's syndrome discussed above is not clear. By some observers the two conditions are held to be identical, whereas others suggest that the absence of genital hypertrophy in Cushing's syndrome differentiates it. Removal of the adrenal tumor has been shown to relieve the condition. As stated previously, Cushing believes that both the hyperplasia of the adrenal cortex and the arterial hypertension may be due to an increase of basophil cells in the pituitary, either hyperplasia or adenoma. Cushing's argument in regard to this question seems somewhat less valid in view of the finding of pituitary basophilic adenoma in from 7 to 8 per cent of routine autopsies at the Mayo Clinic, many of such patients having had absolutely no symptoms during life. Whatever the relationship between these two conditions, there are certainly clinical instances of persistent hypertension associated with primary cortical tumor of the adrenal.

Ovary: The frequent association of hypertension with post-meno-

pausal symptoms suggests the possibility that ovarian atrophy may have some etiological significance. Certainly, the proportion of patients with hypertension at the time of the menopause seems greater than one would expect if there were no such causal relationship. It may be related to the obesity characteristic of the period, or in some way, with the apparent irritability of the vasomotor system. The hypertension has been little affected by sufficient estrin to relieve all symptoms of the menopause. It has been shown that so-called castration cells appear in the anterior lobe of the pituitary following the menopause; whether these are acidophilic or basophilic seems controversial, but if they are the latter, following the argument of Cushing, one might ascribe menopausal hypertension to a pituitary basis. Mention might be made of the rare masculinizing tumors of the ovaries, the so-called arrhenoblastomas, which produce a clinical picture strongly suggestive of adrenal-cortical syndrome but apparently without hypertension.

It is interesting to note that in the experimental hypertension produced by partial occlusion of the renal arteries, as reported by Goldblatt[1], it has been demonstrated by Page[24] that total hypophysectomy does not prevent the development of such ischemic hypertension although it does reduce the blood pressure in animals suffering from this condition. This is suggestive, at least, that in this type of hypertension, the pituitary is not necessary as an etiological factor. However, it has been shown that even the persistence of small amounts of the adrenal cortex or the use of adequate supportive and substitution therapy in cases of bilateral adrenalectomized animals is necessary before hypertension can be produced by renal ischemia. This suggests that the adrenal-cortical hormone plays a part in conjunction with the hypothetical substance produced in the kidney in the pathogenesis of this type of hypertension.

In summary, therefore, it seems apparent that the endocrine mechanism plays a part in the physiological control of blood pressure and that certain obvious states of endocrine dysfunction are related to variations of pressure of pathological degree.

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TREATMENT OF WEBBED FINGERS

Syndactylism

Report of a Case

JAMES A. DICKSON, M.D.

Probably the most generally adopted method of treating syndactylia is that suggested by Didot which consists of incisions on the volar and dorsal sides of the involved fingers. The flaps of skin are raised, leav-

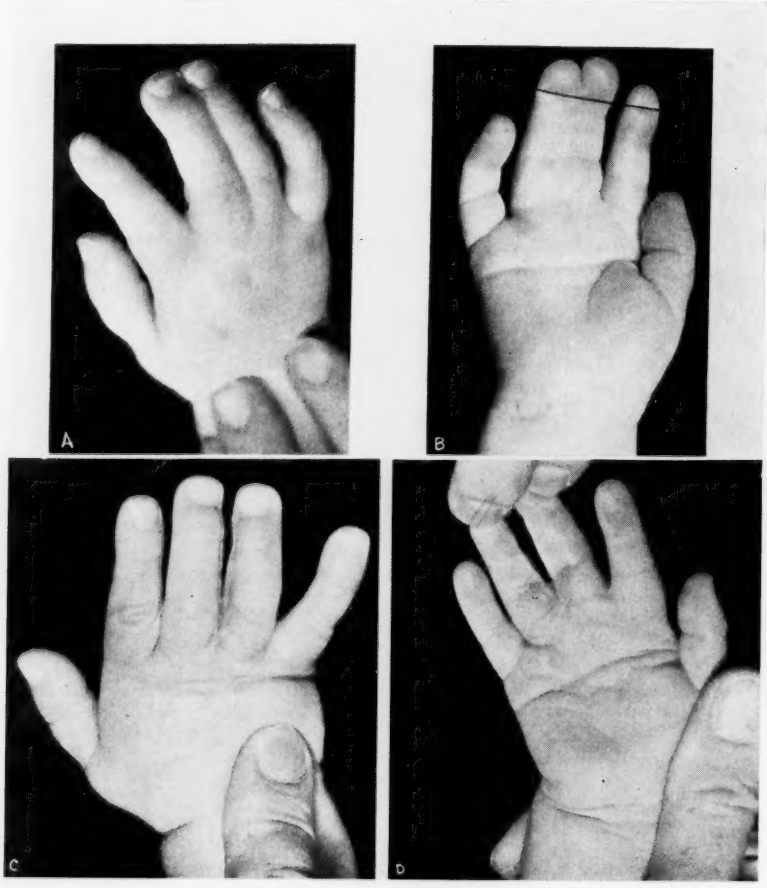

FIGURE 1

A. Photograph showing posterior view of syndactylia of ring and middle fingers of the right hand before operation.

B. Photograph showing anterior view of syndactylia of ring and middle fingers of the right hand before operation.

C. Photograph showing posterior view of the right hand three weeks after operation.

D. Photograph showing anterior view of the right hand three weeks after operation.

ing their bases laterally on opposite sides. When the flaps are sufficiently freed, they are sutured to the skin at the middle of the volar side on one finger and at the middle of the dorsal side on the other. The greatest difficulty consists in obtaining a sufficient amount of skin and it has been my experience that, to obtain a complete covering, many difficulties are encountered.

It is my impression that these can best be handled by means of free full thickness or thick split grafts obtained from the thigh as illustrated in the following case:

The child, 2 years of age, had syndactylism involving the middle and ring fingers of both hands. The method of treatment is demonstrated only for the right hand, a similar procedure being adopted for the left. Figure 1, A and B, shows the webbing of the ring and middle fingers prior to operation.

Under avertin and gas anesthesia, the web between the involved fingers was completely divided, the incision being carried well back in order to form a normal fold at the base of the fingers. A thick split graft was then procured from the thigh and it was further prepared by making multiple holes in it with a sharp bistoury knife, to permit the escape of any serum and assure the taking of the graft. The graft was

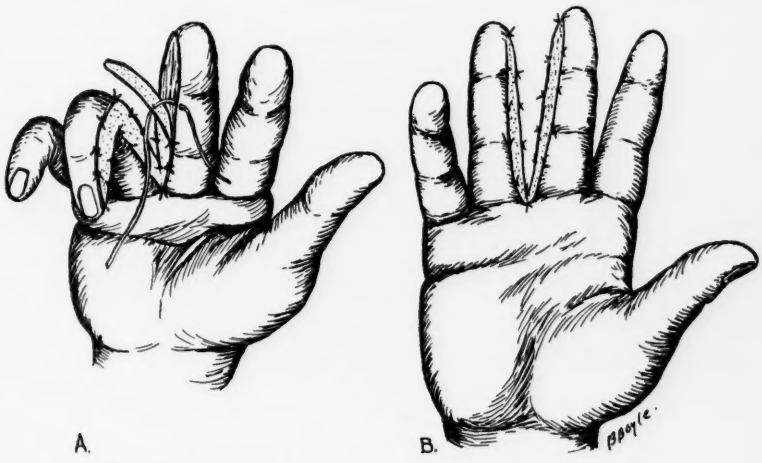

FIGURE 2: Drawing showing technic for correction of syndactylia.

A. Drawing showing full thickness graft being sewed into denuded area with fold at base of fingers.

B. Graft in place before tips of fingers are stitched together to act as splint.

then shaped to the size of the skin defect and sewed into position with fine silk with the fold in the graft at the base of the fingers (Fig. 2, A and

B). After the graft had been accurately secured in position, a stitch was placed through the ends of the fingers to hold them together and cause pressure on the grafts. No dressing was placed between the fingers. At the end of 10 days the stitches were removed and it was found that the graft had taken completely. Figure 2, C and D, shows the hand three weeks after operation.

The results of this form of treatment have been extremely gratifying and the fingers have been more normal than I have been able to secure by any method previously adopted.

The Frank E. Bunts Institute

The Frank E. Bunts Institute will present a course in "Benign and Malignant Tumors" on Monday, Tuesday, and Wednesday, April 3, 4, and 5, 1939.

The program of the course and an application blank will be found on the succeeding pages of this Quarterly.

PROGRAM

BENIGN AND MALIGNANT TUMORS

Monday, April 3, 1939

8:30 A. M.— 9:00 A. M.	Registration	
9:00 A. M.—	Welcome	
9:00 A. M.—10:00 A. M.	Diagnosis and Treatment of Brain Tumors	W. J. Gardner, M. D.
10:00 A. M.—10:30 A. M.	Tumors of the Orbit	A. D. Ruedemann, M. D.
10:30 A. M.—11:00 A. M.	Benign and Malignant Tumors of the Nose and Sinuses	Paul M. Moore, M. D.
11:00 A. M.—11:30 A. M.	Laryngeal Tumors	Justin M. Waugh, M. D.
11:30 A. M.—12 Noon	Tumors of the Jaws	C. A. Resch, D. D. S.
12:00 Noon— 1:00 P. M.	Luncheon	
1:00 P. M.— 1:30 P. M.	Tumors of the Lip and Tongue	Geo. H. Curtis, M. D.
1:30 P. M.— 2:30 P. M.	Tumors of the Neck	R. S. Dinsmore, M. D.
2:30 P. M.— 3:00 P. M.	Mediastinal Growths	B. H. Nichols, M. D.
3:00 P. M.— 3:30 P. M.	Tumors of the Lung	A. C. Ernstene, M. D.
3:30 P. M.— 4:15 P. M.	Benign and Malignant Tumors of the Skin—Pre-cancerous Lesions	E. W. Netherton, M. D.
4:15 P. M.— 5:00 P. M.	Tumors of the Vertebral Column and Spinal Cord	A. T. Bunts, M. D.
6:30 P. M.—	Dinner	
8:15 P. M.—	Guest Speaker—Subject to be announced.	

Tuesday, April 4, 1939

9:00 A. M.— 9:30 A. M.	Esophageal Lesions—Differential Diagnosis	E. N. Collins, M. D.
9:30 A. M.—10:30 A. M.	The Diagnosis of Early Lesions of the Stomach—Use of the Gastroscope	R. J. F. Renshaw, M. D.
10:30 A. M.—11:30 A. M.	Diagnosis of Neoplasms of the Colon	E. N. Collins, M. D.
11:30 A. M.—12:15 P. M.	Roentgen Interpretation of Gastro-Intestinal Lesions	J. C. Root, M. D.
12:15 P. M.— 1:00 P. M.	Luncheon	
1:30 P. M.— 2:30 P. M.	Surgical Treatment of Carcinoma of the Colon and Rectum	T. E. Jones, M. D.
2:30 P. M.— 3:30 P. M.	Malignancy in Relation to Blood Diseases	Russell Haden, M. D.
3:30 P. M.— 4:00 P. M.	Bone Tumors—Benign	J. I. Kendrick. M. D.
4:00 P. M.— 4:30 P. M.	Bone Tumors—Malignant	J. A. Dickson, M. D.
4:30 P. M.— 5:00 P. M.	Endocrine Aids in the Diagnosis of Tumors	E. P. McCullagh, M. D.
6:30 P. M.—	Dinner	
8:15 P. M.—	Guest Speaker—Subject to be announced	

Wednesday, April 5, 1939

9:00 A. M.— 9:30 A. M.	Tumors of the Breast—Diagnosis and Treatment	George Crile, Jr., M. D.
9:30 A. M.—10:30 A. M.	The Pathological Interpretation of End Results in Treatment of Cancer of the Breast	Allen Graham, M. D.
10:30 A. M.—11:30 A. M.	The Rôle of X-ray Therapy in Malignancy	U. V. Portmann, M. D.
11:30 A. M.—12:00 Noon	Cancerphobia	C. L. Hartsock, M. D.

Wednesday, April 5, 1939—Continued

12:00 Noon— 1:15 P. M.	Luncheon	
1:15 P. M.— 1:45 P. M.	The Biophysical Theory of Cancer	Otto Glasser, Ph.D.
1:45 P. M.— 2:30 P. M.	Tumors of the Kidney	W. E. Lower, M. D.
2:30 P. M.— 3:15 P. M.	Bladder and Ureteral New Growths	W. J. Engel, M. D.
3:15 P. M.— 4:00 P. M.	Tumors of the Testes and Prostate	C. C. Higgins, M. D.
4:00 P. M.— 4:45 P. M.	Tumors of the Pelvis—Diagnosis and Treatment	T. E. Jones, M. D.

REGISTRATION BLANK

....., 1939

THE FRANK E. BUNTS INSTITUTE
Cleveland Clinic
Cleveland, Ohio

Gentlemen:

Please register me for the course in "Benign and Malignant Tumors" which is to be given April 3, 4, and 5, 1939.

I am enclosing a check for $5.00 and the remainder of the fee, $5.00, will be paid on registration, April 3.

Name .....

Address .....

.....
Medical School from which Graduated

Note: Checks should be made payable to The Frank E. Bunts Institute and sent to A. D. Ruedemann, M. D., Cleveland Clinic, Cleveland, Ohio.

Exhibits

* * *

Lesions of the Esophagus ..... E. N. Collins, M. D.

Tumors of the Orbit ..... A. D. Ruedemann, M. D., and R. J. Kennedy, M. D.

Tumors of the Neck ..... R. S. Dinsmore, M. D.

Tumors of the Gastro-Intestinal Tract ..... J. C. Root, M. D.

Carcinoma of the Colon and Rectum ..... T. E. Jones, M. D.

Tumors of the Kidney ..... W. E. Lower, M. D.

Tumors of the Bladder and Ureters ..... W. J. Engel, M. D.

Tumors of the Testes and Prostate ..... C. C. Higgins, M. D.

Lesions of the Breast ..... George Crile, Jr., M. D.

Bone Tumors ..... J. A. Dickson, M. D., and J. I. Kendrick, M. D.